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Video Interview

HIV Development Assistance and Adult Mortality in Africa

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THE UNITED STATES' FINANCIAL commitment to health improvement in poor countries is at an all-time high. From just over \$1 billion dollars in 2000, the US budget for global health in 2009 topped \$8.3 billion.¹⁻³ The majority of this increase was directed assistance for disease-specific initiatives such as the President's Emergency Plan for AIDS Relief (PEPFAR), the President's Malaria Initiative (PMI), and the Global Fund to Fight AIDS, Tuberculosis and Malaria.^{1,3} The largest among these, PEPFAR, targeted the rapidly expanding HIV epidemic with a coordinated effort to increase human immunodeficiency virus (HIV) treatment, prevention, and care in 15 focus countries (3 non-African focus countries are not addressed in this analysis). PEPFAR scaled up the delivery of expanded antiretroviral therapy (ART) and supported large-scale prevention efforts.⁴⁻⁷

Although PEPFAR ushered in a new era of support for HIV programs in Africa, its effect on population health has been associated with uncertainty. Some argue that assistance for Africa's HIV sector, led by PEPFAR, has siphoned resources and attention from other health priorities, possibly resulting in worsening health outcomes.⁸ One prior analysis found that PEPFAR was

Context The effect of global health initiatives on population health is uncertain. Between 2003 and 2008, the US President's Emergency Plan for AIDS Relief (PEPFAR), the largest initiative ever devoted to a single disease, operated intensively in 12 African focus countries. The initiative's effect on all-cause adult mortality is unknown.

Objective To determine whether PEPFAR was associated with relative changes in adult mortality in the countries and districts where it operated most intensively.

Design, Setting, and Participants Using person-level data from the Demographic and Health Surveys, we conducted cross-country and within-country analyses of adult mortality (annual probability of death per 1000 adults between 15 and 59 years old) and PEPFAR's activities. Across countries, we compared adult mortality in 9 African focus countries (Ethiopia, Kenya, Mozambique, Namibia, Nigeria, Rwanda, Tanzania, Uganda, and Zambia) with 18 African nonfocus countries from 1998 to 2008. We performed subnational analyses using information on PEPFAR's programmatic intensity in Tanzania and Rwanda. We employed difference-in-difference analyses with fixed effects for countries and years as well as personal and time-varying area characteristics.

Main Outcome Measure Adult all-cause mortality.

Results We analyzed information on 1 538 612 adults, including 60 303 deaths, from 41 surveys in 27 countries, 9 of them focus countries. In 2003, age-adjusted adult mortality was 8.3 per 1000 adults in the focus countries (95% CI, 8.0-8.6) and 8.5 per 1000 adults (95% CI, 8.3-8.7) in the nonfocus countries. In 2008, mortality was 4.1 per 1000 (95% CI, 3.6-4.6) in the focus countries and 6.9 per 1000 (95% CI, 6.3-7.5) in the nonfocus countries. The adjusted odds ratio of mortality among adults living in focus countries compared with nonfocus countries between 2004 and 2008 was 0.84 (95% CI, 0.72-0.99; $P=.03$). Within Tanzania and Rwanda, the adjusted odds ratio of mortality for adults living in districts where PEPFAR operated more intensively was 0.83 (95% CI, 0.72-0.97; $P=.02$) and 0.75 (95% CI, 0.56-0.99; $P=.04$), respectively, compared with districts where it operated less intensively.

Conclusions Between 2004 and 2008, all-cause adult mortality declined more in PEPFAR focus countries relative to nonfocus countries. It was not possible to determine whether PEPFAR was associated with mortality effects separate from reductions in HIV-specific deaths.

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associated with a reduction in HIV-specific mortality.⁹ Beyond HIV, however, PEPFAR's effect remains mostly unknown. Some found evidence to suggest that HIV development assistance displaced funding for other health priorities¹⁰ while other studies failed to find evidence to support the view that PEPFAR's investments crowded out other health measures such as child

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health or antenatal care.¹¹⁻¹³ Whether the unprecedented influx of funds for scaling up HIV treatment and prevention programs was associated with changes in all-cause adult mortality has not been demonstrated.

The relationship between PEPFAR's activities and population health has important policy implications. Limited global health budgets, PEPFAR's expansion to more than a dozen additional countries, and reorganization of US global health aid may signal important changes in the funding environment for HIV programs.^{3,14,15} Understanding the association between PEPFAR and population health outcomes is therefore an important input to the policy-making process with implications for the health of many in sub-Saharan Africa. We studied the relationship between PEPFAR's implementation and trends in adult mortality and further explored whether these trends suggest spillover benefits or unintended harms beyond HIV-related mortality.

METHODS

We performed 2 parallel analyses of changes in adult mortality in areas that received more compared with less PEPFAR support: a cross-country analysis and subnational analyses within Tanzania and Rwanda. Subnational analyses complemented the cross-country analysis by removing some unobserved differences between countries.¹⁶ We chose adult mortality because of its broad importance to population health and because it allowed a comparison with HIV-specific mortality.¹⁷ Methodological and data advances allowed us to analyze adult mortality using individual and household information.¹⁸

Adult Mortality Data

We created a longitudinal data set using person-level information from the Demographic and Health Surveys (DHS). These nationally representative surveys are conducted approximately every 5 years in many low- and middle-income countries by ICF International in collaboration with in-country partners. Survey households

are chosen using a 2-stage sampling process in which representative clusters are selected from a national sampling frame, and a random sample of households is selected within each cluster. In each household, women between 15 and 49 years old who consented were interviewed. The informed consent process typically involved verbal consent from the participants, presumably because illiteracy rates are high in many of the regions in which the DHS are conducted. Sampling was independently repeated in each survey wave. Response rates were greater than 90% in 36 of 41 surveys and never lower than 85%.^{19,20}

We used information on sibling survival provided in the "Maternal Mortality" module. In this module, index women respondents were asked about all children born to their biological mothers, including the age of each living sibling and the date and age at death for each deceased sibling. Using this information, we constructed a longitudinal cohort with repeated observations for each adult sibling (excluding the respondent), indicating whether they died during each year that he or she lived between ages 15 and 59 years. We omitted survey years because of their incomplete observation period. Additional information about the data structure and manipulation appears in the eAppendix (available at <http://www.jama.com>).

We used information from all but 1 of the African DHS conducted after 1998 with maternal mortality modules, yielding a sample from 27 countries: 9 focus countries, including Ethiopia, Kenya, Mozambique, Namibia, Nigeria, Rwanda, Tanzania, Uganda, and Zambia; and 18 nonfocus countries, including Benin, Burkina Faso, Cameroon, Chad, Congo, Democratic Republic of the Congo, Gabon, Guinea, Lesotho, Liberia, Madagascar, Malawi, Mali, Niger, Senegal, Sierra Leone, Swaziland, and Zimbabwe. Three focus countries (Botswana, South Africa, and Côte d'Ivoire) did not have suitable data. We excluded Nigeria's 1999 survey because of questionable

data validity.²¹ Data collection for the surveys used in this study started in November 1998 and ended in May 2010. However, the study's last year of analysis was 2008 because surveys from only 2 countries (Lesotho and Tanzania) contain data for all of 2009, and there were no data from any of the study countries for 2010. We included information on all siblings with complete survival information from 1998 through 2008 (TABLE 1). Sibling survival information for Tanzania and Rwanda were also used in subnational analyses.

PEPFAR Program Intensity

PEPFAR's selection criteria for focus countries were not explicit but appeared to be related to HIV prevalence, the focus countries' governmental commitment to fighting HIV, administrative capacity, and a willingness to partner with the US government and nongovernmental implementers. Country choice, however, is only partially explained by observed factors. For example, Ethiopia was selected despite a low HIV prevalence compared with many African countries (2%), while Malawi was not selected despite a high burden and responsive government. Thus, selection as a focus country, while not random, did not, *ex ante*, suggest straightforward differential trends in mortality among the focus countries. In the cross-country analyses, we compared focus countries with nonfocus countries.

Within countries, we obtained information on the location of PEPFAR-supported clinics and the number of patients receiving PEPFAR-supported ART by clinic (available by request). This information was only available for Rwanda and Tanzania. We analyzed information for both countries' major administrative divisions, 22 regions in Tanzania and 30 districts in Rwanda (we use *district* throughout in this context). Using this information, we calculated 2 measures of district-level program intensity: the annual number of people newly starting ART per capita in the district, and the

annual number of people starting ART per PEPFAR-supported clinic in the district. We then evaluated mortality in districts with above-median PEPFAR-supported programmatic activity compared with below-median districts.

Statistical Analysis

We used logistic regression and a difference-in-difference study design to estimate how the odds of death for adults (defined as men and women ages 15 to 59 years) living in focus countries changed during PEPFAR's implementation relative to those who lived in nonfocus sub-Saharan countries.^{22,23} The difference-in-difference design es-

timates the relative change in mortality over time associated with PEPFAR as the difference of 2 differences: the mortality difference between the focus and nonfocus groups of countries, and the difference in mortality before and after PEPFAR's implementation within each group. This design is well suited for policy evaluations by isolating the effects where the policy was implemented (focus countries) relative to a "control" group (nonfocus countries) and to preexisting trends. (Additional details are available in the eAppendix.)

We used a parallel analytic framework within Tanzania and Rwanda. We identified PEPFAR's programmatic in-

tensity at a district level and compared those districts with above-median programmatic intensity with those with below-median intensity. Throughout, we considered calendar-year 2004 to be the first full year of PEPFAR activities.

The main outcome variable was a binary indicator of whether an adult who was alive for any part of a year died during the year of observation. The main parameter of interest was the coefficient on an indicator of whether the person lived in a focus country during PEPFAR's implementation. All models included year and country (or district) fixed effects, which control for fixed unobserved differences across countries (or districts) and for changes over time that are common to all countries (or districts). Adjusted analyses also included individual characteristics (sibling age in years, recall period between the year of survey and year of observation, and the index woman's education and place of residence) and time-varying country characteristics (HIV prevalence,²⁴ per capita development assistance for health from all sources other than PEPFAR,² gross domestic product per capita,²⁵ and an index of government effectiveness from the World Governance Indicators²⁶). Our specified threshold of significance was $P < .05$, and all tests were 2-sided. We calculated robust standard errors clustered by country to relax the assumption of independent and identically distributed errors within countries.²²

Adult and HIV-Specific Deaths Averted

To examine the possibility of mortality spillovers associated with PEPFAR, we computed the implied number of all-cause adult deaths averted from 2004 to 2008 and an estimate of HIV-specific deaths averted in the same focus countries over the same time period obtained from modeled data. The number of all-cause adult deaths averted was estimated using a 3-step process. First, we predicted the probability of death for all individuals in the focus

Table 1. Study Countries, Participants, and Group Designation

Country	Survey Fieldwork Dates	No. of Unique Adults	Observations, No.	No. of Deaths
Focus countries				
Ethiopia	2-5/2000, 4-8/2005	96 980	391 835	2596
Kenya	4-9/2003, 11/2008-2/2009 ^a	73 580	491 521	2971
Mozambique	8/2003-1/2004	41 103	189 752	1367
Namibia	9-12/2000, 10/2006-3/2007	64 382	340 338	3303
Nigeria ^b	6-10/2008	122 815	1 020 435	4590
Rwanda	6-8/2000, 2-7/2005	74 818	316 179	2943
Tanzania	10/2004-2/2005, 12/2009-5/2010 ^a	83 992	615 367	2993
Uganda	9/2000-3/2001, 4-10/2006	62 132	301 234	2856
Zambia	11/2001-5/2002, 4/2007-1/2008	60 014	328 837	4228
Nonfocus countries				
Benin	8-11/2006	64 463	449 155	1703
Burkina Faso	11/1998-3/1999, 6/2003	55 416	206 068	1123
Cameroon	2-8/2004	41 422	222 637	1550
Chad	7-12/2004	20 891	111 943	736
Congo	1-11/2005	28 305	175 576	1323
Congo Dem Rep	1-8/2007	38 637	295 800	1887
Gabon	7/2000-1/2001	22 083	43 671	210
Guinea	5-7/1999, 2-6/2005	44 848	177 877	977
Lesotho	9/2004-1/2005, 10/2009-1/2010 ^a	47 185	334 908	4428
Liberia	12/2006-4/2007	23 052	178 489	842
Madagascar	11/2003-3/2004, 11/2008-8/2009 ^a	107 869	844 146	3509
Malawi	7-11/2000, 10/2004-1/2005	84 041	305 436	3945
Mali	1-5/2001, 5-12/2006	92 775	470 612	2161
Niger	1-5/2006	34 858	243 442	942
Senegal	2-5/2005	55 881	347 114	1096
Sierra Leone	4-6/2008	19 675	165 810	891
Swaziland	7/2006-2/2007	18 458	128 135	1739
Zimbabwe	9-12/1999, 8/2005-2/2006	58 937	247 359	3394

^aThe fieldwork (data collection) for these surveys was carried out after the end of the study period at the end of 2008 through May 2010. However, the study's last year of analysis was 2008 because surveys from only 2 countries (Lesotho and Tanzania) contain data for all of 2009, and there were no data from any of the study countries for 2010. Each fieldwork date range represents an individual survey.

^bAnother Demographic and Health Survey with data on adult mortality was conducted in Nigeria in 1999. However, the survey's data quality was shown to be poor, and we did not include the survey in the analysis.

countries from 2004 through 2008 using the main adjusted regression coefficients for 2 scenarios: an “actual” scenario where PEPFAR was implemented and a “counterfactual” scenario where it was not implemented. We then calculated the mortality benefit associated with PEPFAR as the mean of the difference between the 2 scenarios for each focus country from 2004 through 2008. Finally, we estimated the number of deaths averted by multiplying that difference by the size of the adult population. This approach relies on the regression parameters to estimate the mortality counterfactual in the absence of PEPFAR.

We calculated the number of HIV-specific deaths averted using previous estimates of PEPFAR’s HIV-specific mortality benefits.⁹ This approach relied on estimates of HIV-specific deaths provided by epidemiologic models developed by the Joint United Nations Programme on HIV/AIDS (UNAIDS). The annual reduction in HIV-specific deaths of 10.5% (95% CI, 4.4%-16.6%) was used to calculate the counterfactual estimate of HIV-specific deaths among adults 15 years and older. (Additional details are available in the eAppendix.) The data sources for estimating all-cause mortality and HIV-specific mortality are different. Unlike the direct estimates of all-cause adult mortality from person-level data used in this analysis, UNAIDS estimates of HIV-specific mortality rely on a mathematical model that combines HIV prevalence with demographic information, HIV natural history, and treatment availability. Although the approaches for using these data sources to estimate the all-cause and HIV-specific mortality benefits associated with PEPFAR share fundamental insights, the differences in the underlying data prevent a direct comparison of these benefits.

Additional sensitivity analyses are available in the eTables and eFigures. These include repeating the analysis while leaving out each country in turn, with only those countries with data both before and after the implementation of

PEPFAR, which spans the year 2004 (the first full year of PEPFAR’s implementation), with only the most recent survey for each country, with only those countries for which data extends at least through 2007, and using linear time trends. We also explored the possibility that preexisting trends account for the differential decline among the focus countries by interacting year dummies with the focus country indicator.

The study was exempted from human subjects review by Stanford’s institutional review board because the data were collected by the DHS project and were not individually identifiable. All analyses were done using Stata version 11.2 (StataCorp).

RESULTS

Cross-Country Analyses

We assembled data on 1 538 612 African adults collected from 41 surveys conducted in 27 countries between 1998 and 2008 (8 943 676 person-years of observation). During this time period, 60 303 deaths were captured in the DHS used in this study. Table 1 shows the survey dates, number of adults, and number of deaths by country. Group comparisons (TABLE 2) show that in 1998, mean HIV prevalence was 8.1% in the focus countries and 6.5% in the nonfocus countries ($P = .62$); mean HIV development assistance per person living with HIV was \$3.80 in focus countries and \$6.30 in nonfocus countries ($P = .55$). Data for nonstudy sub-Saharan countries are also shown. By 2008, mean assistance was \$171.00 per person living with HIV in focus countries and \$76.90 in nonfocus countries ($P = .007$). Trends in HIV assistance per country, shown in FIGURE 1, exhibit an accelerating separation between the focus and nonfocus countries from 2004 to 2008.

Annual age-adjusted all-cause adult mortality aggregated for the focus and nonfocus countries is shown in FIGURE 2. The figure shows relatively greater mortality declines among adults living in focus countries between 2004 and 2008. The figure shows that adult mortality in the focus countries de-

clined from 8.30 per 1000 adults (95% CI, 8.04-8.57) in 2003 to 4.10 per 1000 (95% CI, 3.60-4.61) in 2008. The mortality trends in nonfocus countries did not show a similar decline during the study period (from 8.5 in 2003 to 6.9 in 2008). The country-level mortality trends are shown in eFigure 1.

These divergent trends under PEPFAR are also reflected in the regression analyses. Our unadjusted analyses suggest that between 2004 and 2008 (under PEPFAR), the odds ratio (OR) of death among adults living in focus countries was 0.80 (95% CI, 0.68-0.95; $P = .01$) compared with adults living in nonfocus countries (TABLE 3). After adjustments for country-level and personal characteristics, the mortality OR was 0.84 (95% CI, 0.72-0.99; $P = .03$). Each 1% increase in HIV prevalence was associated with an OR for death of 1.07 (95% CI, 1.01-1.14; $P = .03$), and each 1-point increase in the government effectiveness index was associated with an OR for death of 0.58 (95% CI, 0.38-0.89; $P = .01$). Age of the observed sibling showed a positive association with mortality (OR, 1.05 per year; 95% CI, 1.04-1.05; $P < .001$), while the index woman’s education and residence in an urban environment were negatively associated with mortality (OR, 0.98 per year of education; 95% CI, 0.98-0.99; $P = .01$; and OR, 0.94 for living in an urban environment; 95% CI, 0.89-0.99; $P = .05$). Gross domestic product per capita and non-PEPFAR development assistance for health were not associated with adult mortality.

An analysis of preexisting trends showed that PEPFAR’s onset was associated with a decline in mortality relative to the preexisting trend prior to the program’s onset (eFigure 2). This is consistent with the increasing treatment availability over time in the focus countries.

Subnational Analyses

District-level data for Tanzania and Rwanda are shown in eTable 1. High and low PEPFAR activity districts had similar populations, but program intensity

was significantly different between the groups. We examined district-level changes in adult mortality in areas with low and high programmatic activity using the same framework employed in the cross-country analysis. FIGURE 3 shows adult mortality in Tanzania by 2 groups of districts: above-median and below-median PEPFAR-supported ART per capita. The mortality ORs among adults living in the regions with above-median PEPFAR intensity compared with adults living in regions with below-median intensity between 2004 and 2008 were 0.83 (95% CI, 0.72-0.97; $P = .02$) in Tanzania and 0.75 (95% CI, 0.56-0.99; $P = .04$) in Rwanda (eTable 2).

Spillover Mortality Effects

Using the results for each focus country and generalizing to the size of each country's adult population, we estimate that a total of 740 914 all-cause adult deaths were averted (95% CI, 443 318-1 808 601) between 2004 and 2008 in association with PEPFAR

(eTable 3). In comparison, PEPFAR was associated with an estimated 631 338 (95% CI, 249 026-1 060 253) HIV-specific deaths averted during the same period.⁹

Sensitivity Analyses

We reanalyzed the data to explore the results' robustness. Leaving out any 1 country (eTable 4), analyzing only those countries with data both before and after the implementation of PEPFAR (eTable 5), restricting the sample to only the most recent survey (eTable 5), limiting the analysis to only those countries with data up to 2007 (eTable 5), and using a linear time trend rather than a binary indicator for PEPFAR's implementation (eTable 6) resulted in some loss of power but showed consistent direction and magnitude of the main effect.

COMMENT

We provide robust evidence that PEPFAR has been associated with a de-

cline in all-cause adult mortality in the African countries where it operated most intensively. Our study uses direct evidence from surveys and individual-level reports of mortality. Sub-national analyses in Tanzania and Rwanda yield broadly consistent findings. It was not possible to establish whether there were any all-cause mortality benefits related to PEPFAR beyond the HIV-specific mortality benefits. As discussions about the role of US involvement in global health activities evolve, the implications and limitations of these findings deserve further consideration.

Several possible factors may have contributed to PEPFAR's apparent success. First, PEPFAR's investment has been larger than any previous commitment for a single disease. Development assistance for health has grown from about 4% of US development assistance in 1999 to more than 20% by 2008, and PEPFAR accounts for a large share of this growth.¹ Second, PEPFAR's

Table 2. Comparison of Focus Countries and Nonfocus Countries With Each Other and With Nonstudy Sub-Saharan Countries

Parameter	Mean (95% CI)					
	Focus Countries	Nonfocus Countries	P Value ^a	Other Sub-Saharan Countries ^b	P Value ^c	
Population, millions ²⁷	1998	33.6 (5.1 to 62.1)	9.8 (4.5 to 15.0)	.02	10.3 (2.9 to 17.7)	.35
	2008	43.4 (7.8 to 79.0)	12.8 (5.9 to 19.8)	.01	13.6 (4.8 to 22.4)	.30
HIV prevalence among adults 15-49 y old, % ²⁴	1998	8.1 (5.0 to 11.2)	6.5 (2.0 to 11.0)	.62	5.0 (1.1 to 8.9)	.41
	2008	7.5 (3.9 to 11.0)	5.8 (1.9 to 9.8)	.57	5.0 (1.0 to 9.1)	.56
GDP per capita, constant \$ ²⁵	1998	471.3 (98.6 to 844.1)	641.8 (98.7 to 1184.8)	.67	767.2 (152.6 to 1381.9)	.58
	2008	629.1 (115.1 to 1143.1)	654.5 (180.3 to 1128.8)	.95	995.1 (148.4 to 1841.8)	.34
HIV aid per country, millions of \$ ²	1998	6.3 (0.0 to 14.6)	2.0 (-0.1 to 4.2)	.16	1.8 (0.9 to 2.7)	.25
	2008	240.4 (168.7 to 312.3)	24.6 (10.2 to 39.1)	<.001	63.1 (-6.1 to 132.4)	.37
HIV aid per adult with HIV, \$ ^{2,24}	1998	3.8 (1.8 to 5.7)	6.3 (0.2 to 12.3)	.55	18.4 (0.6 to 35.1)	.11
	2008	171.0 (75.8 to 266.3)	76.9 (54.9 to 98.9)	.007	113.1 (40.7 to 185.6)	.89
Antiretroviral coverage, % ²⁴	2003	2.6 (-2.1 to 7.4)	1.9 (-3.1 to 7.2)	.46	1.9 (-2.6 to 6.5)	.68
	2008	55.6 (38.3 to 73.6)	28.6 (16.1 to 41.2)	.04	39.6 (26.6 to 52.5)	.51
Urban residence, % ²⁵	1998	24.0 (15.8 to 32.2)	33.7 (25.4 to 42.0)	.13	38.1 (29.6 to 46.5)	.45
	2008	28.1 (19.0 to 37.2)	38.0 (29.1 to 46.9)	.15	42.4 (33.5 to 51.3)	.43

Abbreviations: GDP, gross domestic product; HIV, human immunodeficiency virus.

^aP values provided from 2-tailed *t* tests on data for the specified year in the focus countries compared with the nonfocus countries.

^bSub-Saharan countries not included in this study are Angola, Central African Republic, Burundi, Djibouti, Eritrea, Somalia, Sudan, Botswana, South Africa, Côte d'Ivoire, Ghana, Guinea-Bissau, the Gambia, and Togo.

^cP values provided for the comparison between the aggregated estimates for all 27 study countries (focus and nonfocus countries) and the sub-Saharan countries not included in the study. This comparison provides a comparison between the countries excluded from the study and those included along the observed metrics.

structure was unusual, with its implementation relying on experienced non-governmental organizations and academic centers that were rewarded for reaching aggressive coverage targets. Finally, PEPFAR's comprehensive approach to scaling up treatment programs enabled a cogent set of related activities such as antiretroviral procurement processes and supply chain management.

Our estimates of all-cause adult deaths averted and HIV-specific deaths averted are consistent with either positive, negative, or no spillover mortality effects associated with PEPFAR. Although the point estimate of the reduction in all-cause adult deaths is larger than the estimated reduction in HIV-related deaths, the confidence intervals overlap broadly. The HIV-specific mortality benefits associated with PEPFAR were obtained from modeled estimates, making their direct comparison with all-cause mortality benefits uncertain.

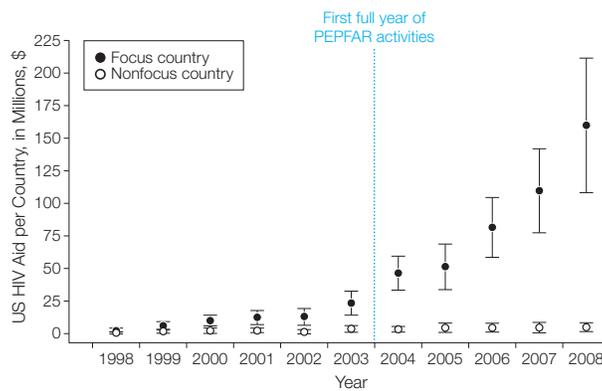
The study's measurements and findings uniquely strengthen the topic's evidence base. A previous study concluded that PEPFAR was not associated with changes in adult mortality.¹² That study, however, relied on more aggregated data from the years 2000 and 2006, limiting its ability to detect relative changes within the study period and not studying benefits that evolved more slowly over time (emerging after 2006, for example). Another study relied on modeled data to estimate mortality benefits, with lingering concerns about data validity.^{9,29} Our use of individual-level data over a longer period of time improves on these limitations and advances the understanding of factors associated with adult mortality. We find that education of the index woman is associated with lower adult mortality. While the literature on the health benefits of personal education is extensive, we show that this effect is additionally present in siblings.^{30,31} We also find that a measure of government effectiveness suggests mortality is lower in coun-

tries with better governance. The association between governance and indicators of population health such as child mortality has been previously demonstrated, but its association with adult mortality has not been well established.³²

Our findings are also notable for the consistent association between HIV development assistance and improve-

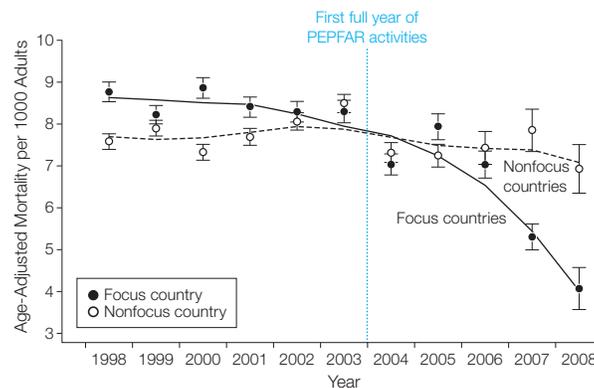
ments in population health when many studies of development assistance programs fail to find meaningful changes in targeted outcomes.^{33,34} Other examples where assistance was associated with its intended goals have also been in the health arena, including smallpox eradication and control of polio.^{35,36} PEPFAR's success with HIV, however, may be the clearest demon-

Figure 1. Trends in Development Assistance for Human Immunodeficiency Virus to Focus Countries and Nonfocus Countries: Mean per-Country Assistance in 2008 US Dollars, 1998-2008



A greater increase in assistance to the focus countries is seen between 2003 and 2004. Data are drawn from the Institute for Health Metrics and Evaluation database.²⁸ We considered calendar-year 2004 to be the first full year of PEPFAR's activities. Error bars indicate 95% CIs; PEPFAR, the US President's Emergency Plan for AIDS Relief.

Figure 2. Age-Adjusted Adult Mortality Trends in the Focus and Nonfocus Countries, 1998-2008



Each point represents the probability that an adult between 15 and 59 years old died during the year per 1000 adults alive for any part of the year. United Nations Population Division age-structured population estimates for each country were used for age adjustments. Age weights were calculated in 5-year age categories from 15 to 59 years (9 age categories). These weights were then used to adjust the crude mortality for each country-year-age group, and the point estimates represent the adjusted total. Mortality declines were greater in the focus countries starting in 2004. A narrow-bandwidth (0.6) loess curve is used to fit the trend. Loess (locally weighted scatterplot smoothing) is a nonparametric method of fitting a curve using local regressions for each point. Error bars indicate 95% CIs; PEPFAR, the US President's Emergency Plan for AIDS Relief.

Table 3. Regression Models Estimating the Odds Ratio of Death in Study Adults in Focus Countries vs Nonfocus Countries

	Unadjusted OR (95%CI) ^a	P Value	Adjusted OR With Country Covariates (95% CI)	P Value	Adjusted OR With Country and Personal Covariates (95% CI)	P Value
Adult death ^b	0.80 (0.68-0.95)	.01	0.83 (0.72-0.95)	.01	0.84 (0.72-0.99)	.03
HIV prevalence (per additional 1%)			1.07 (1.01-1.14)	.03	1.07 (1.01-1.14)	.03
Non-PEPFAR assistance ^c			0.99 (0.96-1.01)	.24	0.99 (0.96-1.02)	.61
GDP per capita (per additional \$1)			1.00 (1.00-1.00)	.65	1.00 (0.99-1.01)	.58
Government effectiveness (per 1-point increase) ^d			0.62 (0.41-0.95)	.03	0.58 (0.38-0.89)	.01
Sibling age (per year)					1.05 (1.04-1.05)	<.001
Residence in urban area ^e					0.94 (0.89-0.99)	.05
Education (per additional year) ^e					0.98 (0.98-0.99)	.01
Recall (interval between survey and observation, per year)					0.97 (0.95-0.99)	.006

Abbreviations: GDP, gross domestic product; HIV, human immunodeficiency virus; OR, odds ratio; PEPFAR, US President's Emergency Plan for AIDS Relief.

^aAll results are exponentiated coefficients on parameters in logistic regression models. Unadjusted model includes the main effect as well as country and year fixed effects. All CIs are calculated using robust standard errors clustered by country.

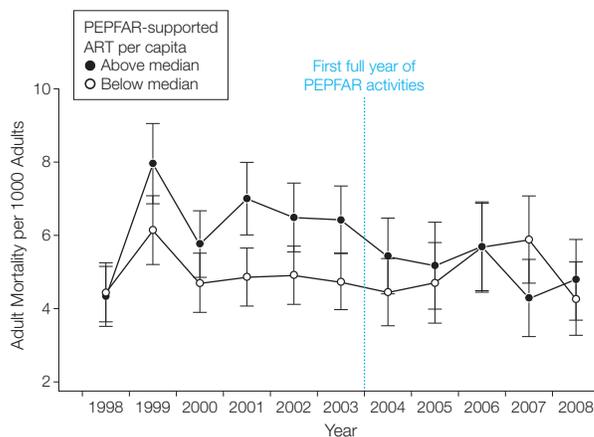
^bThese ORs represent the relative reduction in mortality among adults living in the focus countries while PEPFAR was implemented compared with adults living in nonfocus countries.

^cAll development assistance for health from all donors minus US-funded HIV development assistance per capita.²

^dThe index is centered at 0 and each 1-point represents 1 SD with higher numbers representing greater government effectiveness.²⁶

^eThese variables are characteristics of the index woman rather than the sibling. The residence status and educational status of the sibling are not known.

Figure 3. Adult Mortality Trends in Tanzania Separated by PEPFAR Activity, 1998-2008



PEPFAR activity intensity is measured as the number of people receiving PEPFAR-supported antiretroviral therapy (ART) per capita in the region. We show ART per capita because ART per clinic may partially reflect the pre-existing clinic structure in the district; ie, a district with a few large clinics may appear to have greater intensity than a district with the same number of people receiving care in a greater number of smaller clinics. Tanzania is shown because it had a longer period of observation than Rwanda. (Additional trends by clinic size for Tanzania and Rwanda are shown in eFigure 3.) Error bars indicate 95% CIs; PEPFAR, the US President's Emergency Plan for AIDS Relief.

stration of aid's effectiveness in recent years.

Our study has several limitations. First, other factors that coincide with PEPFAR's timing and geographic activity may confound the analysis. Notably, a different epidemic phase between the focus and nonfocus countries could lead to earlier mortality declines in focus countries unrelated to

PEPFAR. Our range of sensitivity analyses investigate this possibility, but we cannot fully rule out the possibility of phase offset. A successful treatment campaign, however, can alter the epidemic phase, maintaining the possible role played by PEPFAR in adult mortality improvements.

Second, past work has shown that adult mortality estimation from sur-

veys is biased by imperfect recall and underrepresentation of high-mortality families.^{18,37} Bias could also be introduced if adult mortality is underestimated in countries with high HIV mortality because of selection against sibships with HIV-infected index women. However, previous analyses suggest that the bias is approximately constant over time, limiting its role in this analysis.¹⁸

Third, not all the focus countries were included in this study. Botswana, South Africa, and Côte d'Ivoire did not have suitable data for this analysis—and the conclusions cannot therefore be generalized to all focus countries. Botswana and South Africa, in particular, carry a heavy HIV burden, and their omission could change PEPFAR's overall effect, although the direction of change is unclear.

Fourth, our subnational analyses cannot fully overcome the concern over unobserved confounders. In addition, we assumed that all siblings live within the same urban/rural environment as the index woman, as well as the same country (for cross-country analysis) or district (for subnational analyses). We do not have evidence for or against this assumption's validity.

In conclusion, we provide new evidence suggesting that reductions in all-

cause adult mortality were greater in PEPFAR's focus countries relative to the nonfocus countries over the time period from 2004 through 2008. Our analysis suggests an association of PEPFAR with these improvements in population health.

Author Contributions: Dr Bendavid had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Bendavid.

Acquisition of data: Bendavid, Holmes.

Analysis and interpretation of data: Bhattacharya, Miller.

Drafting of the manuscript: Bendavid.

Critical revision of the manuscript for important in-

tellectual content: Bendavid, Holmes, Bhattacharya, Miller.

Statistical analysis: Bendavid, Bhattacharya, Miller.

Study supervision: Bhattacharya, Miller.

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