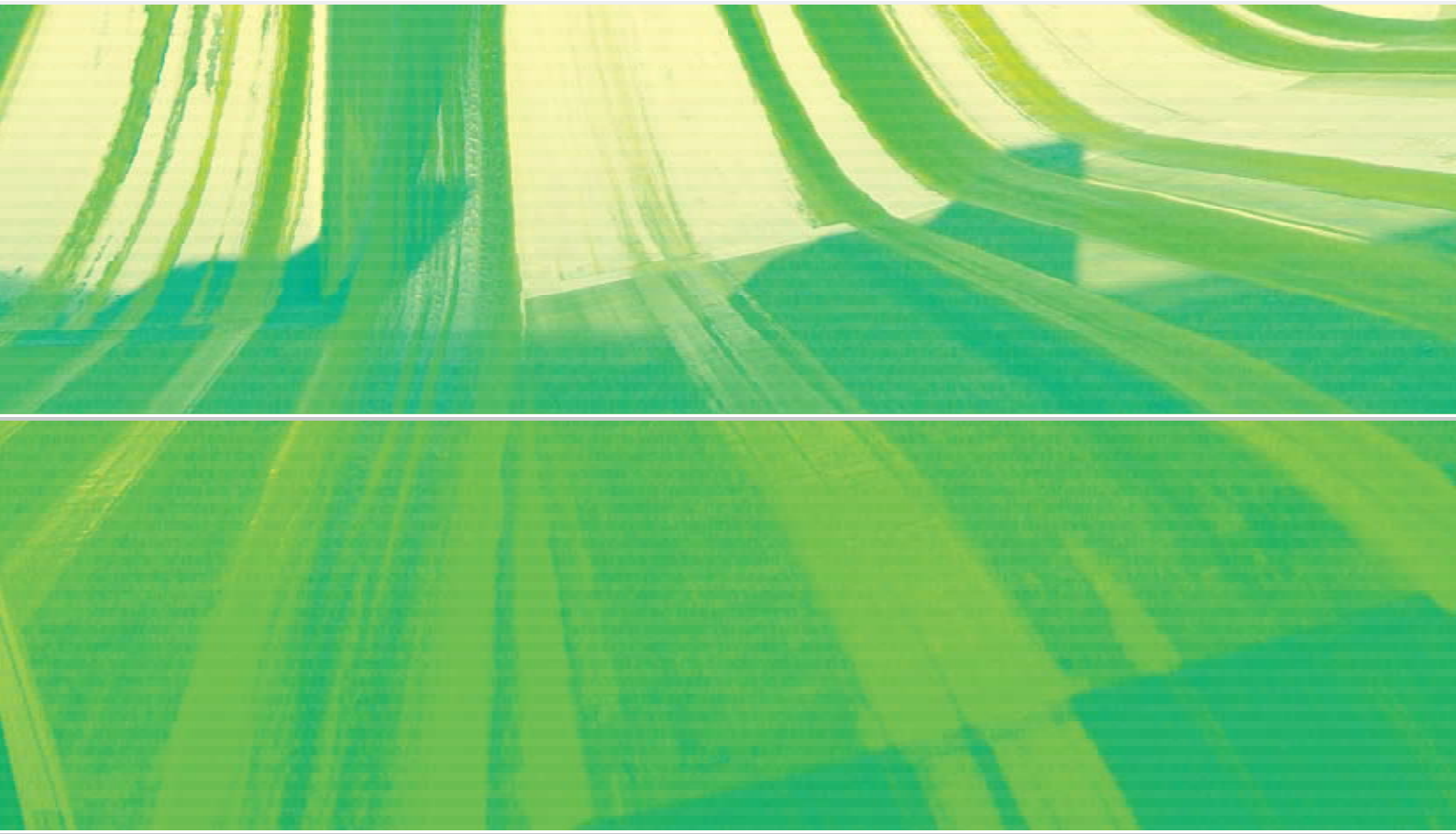
THE GLOBAL FUND TO FIGHT AIDS, TUBERCULOSIS AND MALARIA
THIRD REPLENISHMENT (2011-2013)

FINANCIAL AND HEALTH IMPACTS OF CONTINUED SUPPORT TO THE THREE DISEASES: LONG-TERM ESTIMATES



Investing in our future
The Global Fund
To Fight AIDS, Tuberculosis and Malaria

LIST OF ABBREVIATIONS

ARV	antiretroviral
PEPFAR	President's Emergency Plan for AIDS Relief (U.S.)
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization

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EXECUTIVE SUMMARY

1. By the end of 2011, programs financed by the Global Fund will provide antiretroviral (ARV) therapy to 3.5 million people. 220 million insecticide-treated nets or long-lasting insecticidal nets to protect against malaria will have been distributed, and 1.8 million care and support services will be provided to orphans and other vulnerable children in 2011 alone. The costs and expected health impact of maintaining the support to these recipients have been projected until 2020. The projections include total program costs met by domestic contributions as well as external contributions.

2. Behavior of the cohorts of beneficiaries was projected over time through 2020, using established epidemiological models[1]. Program-level recurrent costs of maintaining supporting health services were calculated using estimates of the current marginal cost per beneficiary supported, based on comprehensive costing studies available from selected programs, as well as ARV and insecticide-treated net procurement price data.

3. For ARV therapy, the annual program-level cost for the 2011 cohort would decrease slightly from (real) US$ 1.9 billion in 2011 to US$ 1.7 billion in 2020[2]. The increasing cost of second-line treatments is compensated by a decreasing total number of patients. In 2011, 5 percent of patients are assumed to be on the more expensive second-line regimens, accounting for 14 percent or US$ 264 million of overall ARV therapy delivery cost. In 2020, 24 percent of patients are estimated to be on second-line regimens, accounting for 50 percent or US$ 847 million of overall ARV therapy delivery cost.

4. Replacing all long-lasting insecticidal nets that will have been distributed by the end of 2011 every three years is projected to cost an average of US$ 364 million every year. Cost of providing services to the orphans and other vulnerable children receiving such services in 2011 would decrease from US$ 335 million in 2011 to US$ 95 million in 2020, as over half of the orphans and other vulnerable children reach adulthood.

5. The Global Fund share of the overall program-level costs was estimated at 27 percent for ARV therapy, 74 percent for long-lasting insecticidal nets and 16 percent for services for orphans and other vulnerable children, based on grant-reported data on expenditure and service delivery results for the period 2006-2009. ARV therapy is estimated to save around 2.0 million life-years on average per year between 2011 and 2020, and long-lasting insecticidal nets are estimated to save 6.2 million life-years annually.

6. In conclusion, the annual cost of ongoing support for 2011 beneficiaries is fairly stable over the period 2010 to 2020, if current service unit costs are maintained. The Global Fund share of these costs will remain stable if contributions by partners and domestic contributions stay the same. The price of second-line ARVs is a key cost driver, increasingly so over time. This underscores the importance of investing in treatment quality to improve retention of patients on first-line regimens. Management of service delivery unit costs in program implementation (including support to use of generic drugs and drug and commodity price reductions) will also be critical.

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[1] Led by Futures Institute, using methods and assumptions agreed with the Joint United Nations Programme on HIV/AIDS (UNAIDS) Epidemiological Reference Group, for ARV therapy and orphans and other vulnerable children, and by World Health Organization (WHO) Global Malaria Program dept., based on effectiveness estimates according to the Child Health Epidemiology Reference Group, for long-lasting insecticidal nets.

[2] All future costs estimated are presented as real US$ 2009.

INTRODUCTION

7. At the end of 2009, programs financed by the Global Fund were providing ARV therapy to 2.5 million people. From 2004, when the Global Fund began measuring results of the programs it supports, to the end of 2009, Global Fund-supported programs had distributed 104 million insecticide-treated nets and provided 4.5 million basic care and support services to orphans and other vulnerable children – over 1.3 million in 2009 alone. Service delivery targets have been agreed for grants in Rounds 1 to 8 and for approved Round 9 proposals that will start in 2010. By the end of 2011, 3.5 million people are expected to be on ARV therapy, 220 million insecticide-treated nets or long-lasting insecticidal nets will have been distributed, and in 2011 alone, 1.7 million basic care and support services will be provided to orphans and other vulnerable children (see Table 1).

8. At current rates of survival, patients starting ARV therapy today can expect to live for an additional 12 years on average, meaning that they require ARV therapy for 12 years. Long-lasting insecticidal nets need to be replaced every three years to maintain effective protection against malaria [1]. Orphans and other vulnerable children will continue to need support until they reach adulthood. Support for recipients of Global Fund grants should be provided for as long as they need it.

9. This paper presents model-based projections of the funding required to allow 2011 beneficiaries of ARV therapy, long-lasting insecticidal nets and services for orphans and other vulnerable children to continue receiving services as long as they need them. This includes estimates of the corresponding expected health benefits in terms of deaths averted and life-years gained.

Table 1. Service delivery results and targets of Global Fund-supported programs (2008-2011)

		End 2008	Mid 2009	End 2009	2010	2011	*Comments*
Insecticide-treated nets distributed (millions)	**Target**			100	180	**220**	*Cumulative* distributions. Results include both conventional insecticide-treated nets and long-lasting insecticidal nets; from 2009 onwards the majority of insecticide-treated nets procured are long-lasting insecticidal nets.
	Result	70	88	**104**			
Persons alive on **ARV therapy** (millions)	**Target**	1.8		2.4	2.9	**3.5**	People receiving ARV therapy as of reporting date
	Result	2.0	2.3	**2.5**			
Services for orphans and other vulnerable children (millions)	**Target**				6.0	**7.7**	*Cumulative* number of services provided. In 2009, over 1.3 million services were provided.
	Result	3.2	3.7	**4.5**			
Source of targets		Rounds 1-8				Rounds 1-9	

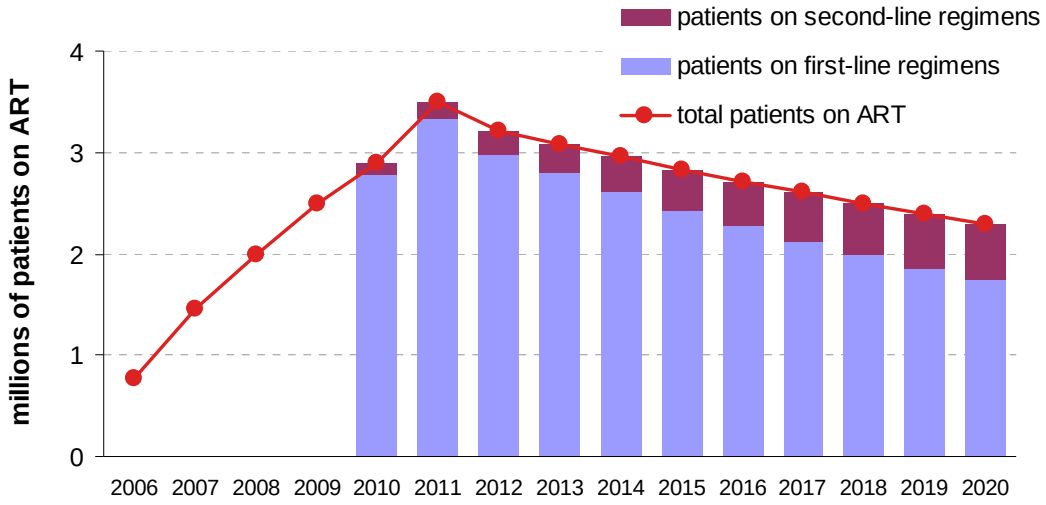
Source: Global Fund Strategic Information database. Results are those of Rounds 1-7 grants. Targets include Round 8 approved grants in 2010 and 2011, and Round 9 approved grants in 2011. These portfolio-aggregate results and targets represent the sum of grant-specific numbers reported by some of the recipients, and national program-level numbers reported by other recipients [8].

BENEFICIARIES OF CURRENT PROGRAMS

10. Future costs and health impact of continued investments are estimated based on projections of cohorts of beneficiaries as of 2011 (see Annex, section A, for description of projection methods).

11. For *ARV therapy*, it was assumed that approximately 80 percent of people survive the first year of treatment and 96 percent survive each subsequent year [2]. This means that of the 3.5 million people expected to be provided with ARV therapy by Global Fund-supported programs at the end of 2011, 2.3 million will still be alive and on treatment in 2020. Today most of these patients are on first-line therapy. However, taking into account the rates of treatment failure reported from low- and middle-income countries, around 550,000 will require more costly second-line regimens by 2020 (Figure 1; see Annex section A for a detailed description of modeling survival on ARV therapy and retention on first-line and second-line regimens).

Figure 1. HIV/AIDS patients on ARV therapy in Global Fund-supported programs according to end-2009 grant results and 2010-2011 grant targets, and retention on first-line and second-line ARV regimens over time



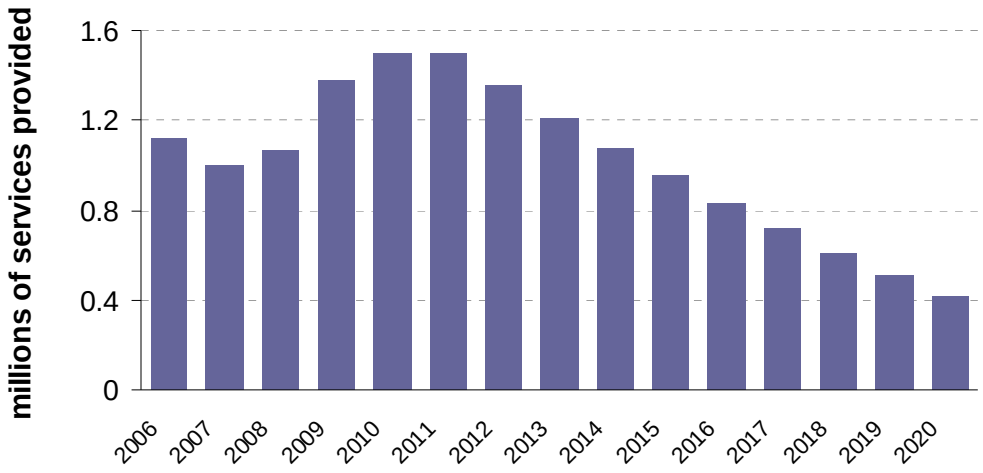
Note: Numbers for 2006-2009 represent aggregate grant-reported results; numbers for 2010-2020 represent projections for the 2011 cohort. Projection as described in [2] and Annex.

12. *Long-lasting insecticidal nets*, the WHO-recommended most cost-effective type of nets, need to be replaced every three years to remain effective. To maintain a total number of 220 million long-lasting insecticidal nets operational (the number of nets that will have been distributed by the end of 2011, according to 2011 grant targets), around 50 million long-lasting insecticidal nets will have to be distributed every year.

13. The Global Fund's *support for orphans and other vulnerable children* is concentrated in Ethiopia, Malawi, Tanzania and Rwanda. These four countries together accounted for the vast majority of the total services provided to orphans and vulnerable children in 2009. Types of support vary between countries, and include combinations of food, clothing, bedding, shelter, health care, education and psychosocial support.

14. Orphans and other vulnerable children need support until they reach the age of 18. By 2020, all children aged 7 and over as of 2010 will have reached the age of 18, but those under age 7 who will still be alive in 2020 will still require support. Assuming the typical age pattern of orphans and other vulnerable children, around 234,000 of the children that received Global Fund support in 2009 will still require support in 2020 (Figure 2).

Figure 2. Services provided to orphans and other vulnerable children by Global Fund-financed programs (end-2009 grant results and 2010-2011 grant targets), and need for continued support over time



Note: Numbers for 2006-2009 represent aggregate grant-reported results; numbers for 2010-2020 represent projections for the cohort supported in 2011.

SERVICE DELIVERY UNIT COSTS

Full National Program-Level Cost

15. The cost per patient-year of ARV therapy, orphans and other vulnerable children supported for a year, and long-lasting insecticidal nets distributed were estimated as shown in Table 2. These costs represent overall, recurrent program-level service delivery costs, to which the Global Fund contributes, alongside other partners and domestic resources.

16. For ARV therapy, a year of first-line treatment for an adult is estimated to cost on average US$ 487, of which ARV drugs make up the largest cost component (US$ 204). Drug costs are based on procurement prices reported by Global Fund-supported countries, whereas the costs of treatment delivery were estimated based on data from comprehensive costing studies available from selected countries (Table 1 and sections B and C of the Annex). Second-line ARV therapy was estimated to cost an average of US$ 1,521 per adult patient-year (of which ARV drugs make up US$ 1,238).

17. The cost per long-lasting insecticidal net distributed was estimated based on country-reported procurement prices (median US$ 5.3). A US$ 2 cost was added per long-lasting insecticidal nets for delivery to households, based on comprehensive costing studies from selected countries.

18. Support to orphans and other vulnerable children was estimated to cost US$ 224 per child per year, based on expenditure data from 300 nongovernmental organizations providing support to orphans and other vulnerable children in 7,400 sites in sub-Saharan Africa [3].

Table 2. Service delivery unit cost assumptions

Service	Component	Program level (US$)	Source
ARV therapy (per patient-year)	First-line ARVs	204#	Global Fund Price & Quality Reporting system and WHO Global Price Reporting mechanism [4, 5]
	Second-line ARVs	1,238#	
	Laboratory	180	Comprehensive costing studies (see Annex, section B)
	Service delivery	103	WHO-CHOICE country estimates [6] (see Annex, section B)
	End-of-life treatment of opportunistic infections	160	During a patient's *last* year on ARV therapy only. Based on WHO-CHOICE [6] and literature review of non-ARV therapy costs of HIV care, *Futures Institute* (see Annex, section C)
	Total first-line ARV therapy	**487#**	
	Total second-line ARV therapy	**1,521#**	
Long-lasting insecticidal nets	Long-lasting insecticidal net procurement	5.3*	Global Fund Price & Quality Reporting system [4]
	Distribution	2.0	Comprehensive costing studies [7]
	Total long-lasting insecticidal net	**7.3**	
Support to orphans and other vulnerable children	**Comprehensive support**	**224**	Data from 300 nongovernmental organizations, 7400 sites in sub-Saharan Africa, with adjustment for expected economies of scale during program scale-up [3]

Notes: See Annex, sections B and C for details of cost estimations.
* For countries with long-lasting insecticidal net procurement price data, the median price in the most recent year of a country's reporting was used; for countries without data the global median price of US$ 5.3 per long-lasting insecticidal net was used.
# ARV and ARV therapy cost assumptions are based on country-specific estimates of ARV and service delivery cost and fixed cost for laboratory and end-of-life treatment of opportunistic infections, weighted by the numbers of patient on ARV therapy in Global Fund-supported programs at end-2009.

Global Fund Share of Program-Level Cost

19. The Global Fund's share of overall service delivery was estimated based on grant expenditure patterns and disbursements compared with grant service delivery results for the following year (Table 3). During the period from 2007 to 2009, the Global Fund contribution was around US$ 130 per patient-year of ARV therapy (as averaged over first- and second-line treatments), US$ 5.4 per long-lasting insecticidal net distributed, and US$ 35 per year of services per orphan or other vulnerable child.

20. It is important to note that countries may define service delivery areas differently. In addition, in most cases the reported service-specific expenditures did not include program management, training, or fixed costs and investments. Hence the overall cost to the Global Fund per supported patient on ARV therapy may be higher than the US$ 130 that recipients reported under the ARV therapy service delivery area.

21. In comparison to the program-level recurrent unit costs, the Global Fund contributes less than one-quarter of the overall cost for each ARV therapy patient (US$ 130 out of approximately US$ 518, as the weighted average program-level cost across patients on first-line and second-line regimens) but nearly the full cost (US$ 5.4 out of U$$ 7.3) for insecticide-treated nets. For services for orphans and other vulnerable children, the average contribution of US$ 35 is much smaller than the estimated cost of US$ 224 of a comprehensive package of support. This may reflect the fact that Global Fund-supported services provided typically include only a selection of the comprehensive package of service (e.g. nutritional support or paying education fees, but not both).

Table 3.Global Fund disbursements and expenditures, by disease area

		2006	2007	2008	2009
Global Fund disbursements		US$ 1,322M	US$ 1,727M	US$ 2,254M	US$ 2,755M
Disbursements: distribution across diseases	HIV	54%	63%	62%	48%
	TB	15%	16%	14%	14%
	Malaria	31%	20%	23%	37%
Expenditures*	ARV therapy as percentage of HIV	23%		25%	
	Long-lasting insecticidal net as percentage of malaria	34%		38%	
	Orphans and other vulnerable children as percentage of HIV	3%		4%	
Estimated Expenditures	ARV therapy	US$ 164M	US$ 274M	US$ 347M	US$ 328M
	Long-lasting insecticidal net	US$ 139M	US$ 134M	US$ 198M	US$ 386M
	Orphans and other vulnerable children	21	44	55	53
Service Deliveries	ARV therapy	0.8M	1.4M	2.0M	2.5M
	Long-lasting insecticidal net	10.4M	27.6M	24.7M	34.0M
	Orphans and other vulnerable children	1.0M	1.3M	1.3M	Over 1.3M
Expenditures per Service Delivery	ARV therapy	US$ 181	US$ 113	US$ 138	US$ 139
	Long-lasting insecticidal net	US$ 10.1	US$ 5.0	US$ 5.4	US$ 5.8
	Orphans and other vulnerable children	US$ 12	US$ 16	US$ 34	US$ 40

* 2006 share based on Enhanced Financial Reporting pre-current reporting period, which is reported in aggregate covering the period for grants generally through 2006. 2007-2009 share based on annualized Enhanced Financial Report current reporting period. Recipients differ in their categorization of service delivery areas and cost components, and certain expenditures related to ARV therapy delivery may not always be classified under ARV therapy. Expenditures per service delivery assume one calendar year lag between disbursement and service delivery reported.

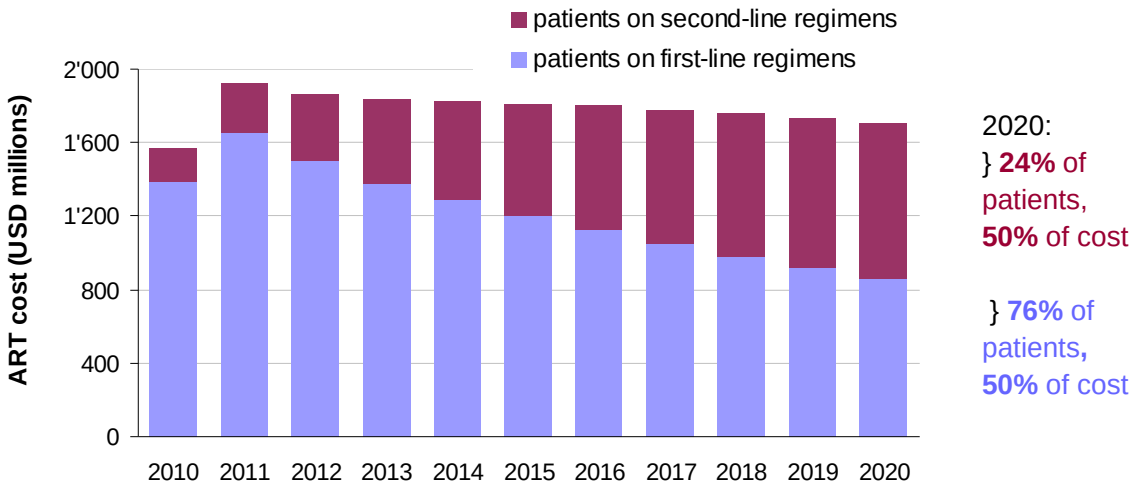
COST OF CONTINUED SUPPORT: 2011 BENEFICIARIES

22. The future cost of continuing to provide ARV therapy to the people who are projected to be on treatment at the end of 2011 is shown in Figure 3. In 2011 alone, the full program-level cost of ARV therapy for these patients is around US$ 1.9 billion. This annual cost declines slightly over time, to reach US$ 1.7 billion in 2020[3]. The reduction is due to a declining total number of patients on treatment, but is partially offset by the fact that an increasing proportion of patients will require more expensive second-line regimens (Figure 1). Because second-line regimens are much more expensive than first-line regimens (based on prices reported by countries in 2008–2009), the small number of patients on second-line regimens account for a large proportion of overall ARV therapy cost: in 2011, the 5 percent of patients on second-line regimens account for 14 percent of ARV therapy cost (US$ 264 million); in 2020, the 24 percent of patients on second-line regimens account for 50 percent of ARV therapy cost (US$ 847 million – see Figure 3).

23. For *long-lasting insecticidal nets*, the cost of three-yearly replacements for all beneficiaries amounts to US$ 364 million every year between 2012 and 2020.

24. *The cost of services for orphans and other vulnerable children* decreases over time, from US$ 336 million in 2010 to US$ 93 million in 2020. The decrease reflects an increase over time in the number of children who reach the age of 18, at which time they are assumed to no longer need support (Figure 2).

Figure 3: ARV therapy cost for people on ARV therapy in 2011 cohort: first-line vs. second-line treatment



Notes: Assumes fixed prices of first-line and second-line ARV regimens over time, fixed distributions of patients over the regimens, and no inflation or discounting.

[3] All future costs estimated are presented as real US$ 2009.

Global Fund Share of Program-Level Costs

25. As a provider of additional funding alongside domestic contributions and those of other donors, the Global Fund supports a part of these total program-level resource needs. If domestic and other donor contributions remained fixed at the level observed between 2007 and 2009, the Global Fund would need resources of US$ 846 million for the three services in 2010 – US$ 377 million (45 percent) for ARV therapy; US$ 409 million (48 percent) for long-lasting insecticidal nets and US$ 60 million (7 percent) for services for orphans and other vulnerable children. The cost of providing ongoing support would fall to US$ 584 million by 2020 – US$ 298 million (51 percent) for ARV therapy, US$ 269 million (46 percent) for long-lasting insecticidal nets and US$ 17 million (3 percent) for services for orphans and other vulnerable children.

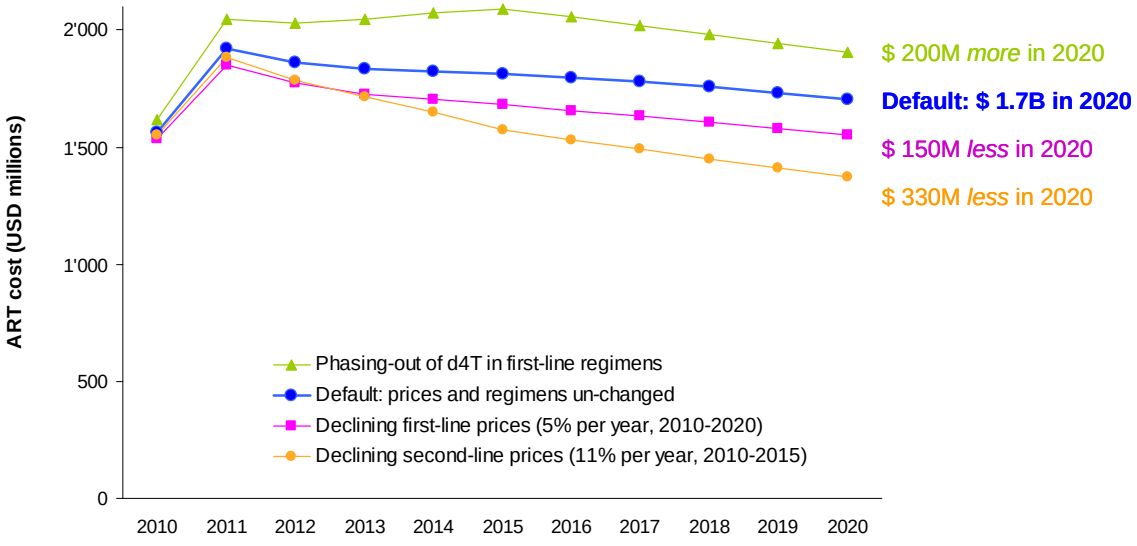
26. However, if domestic or external contributions fell in coming years, the cost to the Global Fund would be higher.

Determinants of Costs: Antiretroviral Prices

27. For ARV therapy, resource needs are influenced by future ARV prices and the distribution of patients over different ARV regimens. Assuming fixed prices, for the 2011 cohort ARV drugs account for 56 percent of total ARV therapy costs through 2010–2020.

28. For first-line ARVs, the phasing out of d4T, the least expensive drug, as per the WHO 2009 treatment recommendations [9], would increase the average cost of first-line drugs per patient-year from US$ 204 to US$ 293 (if patients currently on d4T were moved to alternative regimens), based on the 2008 distribution of patients over various WHO-recommended regimens, and assuming prices remain unchanged. This would result in a US$ 200 million higher ARV therapy financing need in 2020 than in the default projection, for the 2011 cohort (Figure 4).

Figure 4: Effect of changing ARV prices on ARV therapy (program-level) cost

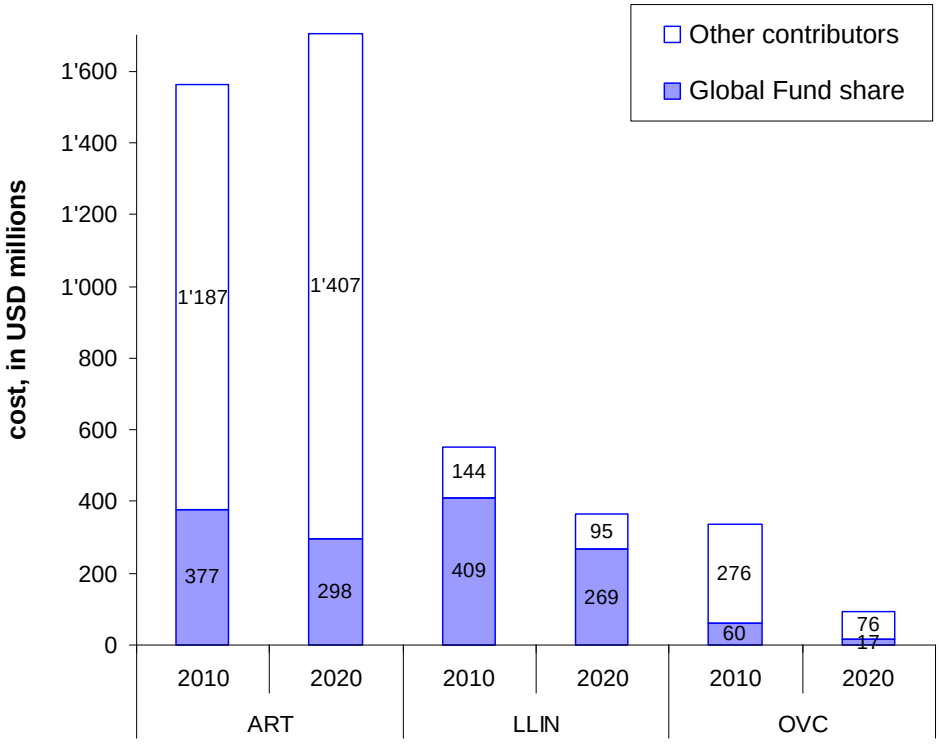


Note: Full program-level cost for the 2011 cohort.

29. On the other hand, between 2006 and May 2009 the median price of first-line ARVs has decreased by 12 percent per year, as a weighted average over the six most commonly used regimens [7]. The Global Fund has committed to a further 5 percent annual price decline in first-line adult ARVs. Assuming a continued 5 percent further annual price decline, the ARV therapy financing need would be US$ 150 million lower in 2020 for the 2011 cohort.

30. For second-line ARVs, prices could decline substantially in coming years, as a larger market develops and competition among manufacturers increases. Such a decrease has recently been observed for pediatric ARVs. A median annual 11 percent price decline from US$ 1,238 in 2009 to US$ 636 from 2015 onwards (similar to that observed for first-line ARVs, which have declined by 12 percent yearly between January 2007 and May 2009 [7]) could reduce the costs in 2020 by US$ 330 million.

Figure 5: Projected (annual) Global Fund share in future program-level costs, for the end-2011 cohort



HEALTH IMPACT

31. Deaths averted and life-years saved through ARV therapy and long-lasting insecticidal nets are shown in Figure 6.

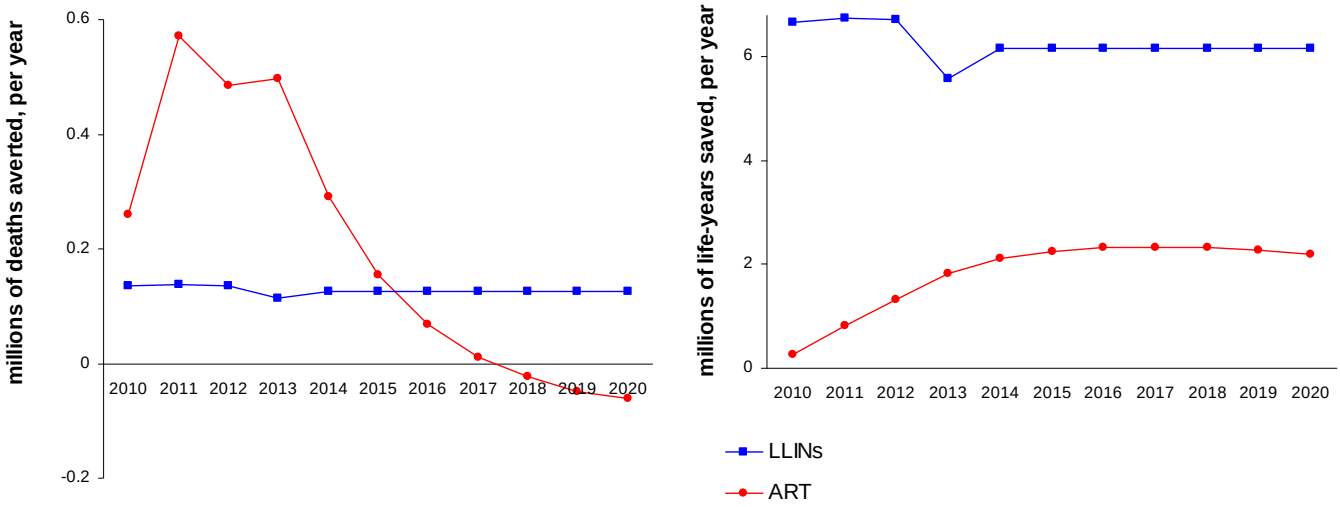
32. For ARV therapy, among patients supported as of 2011, most deaths (520,000) are averted in 2011, the year with the largest number of new patients (Figure 6a). In this cohort, the annual number of deaths averted falls gradually over subsequent years. From 2018 onwards, no additional deaths are averted.

33. The averted deaths correspond to 830,000 life-years saved in 2011, increasing to a fairly stable 2.3 million annual life-years saved by 2017 (Figure 6b). Cumulatively over 2011—2020, ARV therapy is estimated to save 19.8 million life-years by continuing support for the 2011 cohort.

34. Long-lasting insecticidal net distributions at 2011 levels result in around 140,000 deaths averted among children under five in sub-Saharan Africa every year (Figure 6a). This corresponds to an annual 6 million life-years saved (Figure 6b). These numbers are stable over the projection years, reflecting that the number of recipients remains constant. Cumulatively over 2011—2020, long-lasting insecticidal net distributions is estimated to save 63 million life-years by continuing support for 2011 recipients.

35. Compared to ARV therapy, long-lasting insecticidal nets save more life-years per death averted because malaria deaths (prevented by long-lasting insecticidal nets) generally occur at a much younger age than HIV/AIDS deaths (median ages of 1.8 years [10] and 30–35 years, respectively).

Figure 6. Expected health impact: mortality and lives saved from ARV therapy and long-lasting insecticidal nets:
(a) deaths averted and (b) life-years saved



Note: For long-lasting insecticidal nets, life-years saved are attributed to the year of the death averted, with a 3 percent annual discount, resulting in a median 25 life-years saved per death averted. For ARV therapy, in the 2011 cohort no deaths are averted after 2017, as mortality on ARV therapy reaches the mortality rate among the (few) patients not accessing ARV therapy who would have survived until 2017.

DISCUSSION

36. Projections show that the cost of maintaining support for patients on ARV therapy as of 2011 declines slightly from US$ 1.9 billion in 2011 to US$ 1.7 billion in 2020, assuming no further price reductions of first- and second-line ARV drugs. Replacement of long-lasting insecticidal nets would cost US$ 364 million per year, while the cost of providing services to the orphans and other vulnerable children accessing those services in 2011 would decrease from US$ 336 million in 2011 to US$ 93 million in 2020.

37. We have assumed that service delivery unit costs remain the same over time. However, by 2020 ARV therapy cost could be up to 10 percent (US$ 200 million) higher if stavudine (d4T) is gradually phased out in first-line regimens. It could also be 8 percent or 17 percent (US$ 150 million and US$ 330 million) lower, respectively, if prices of first-line and second-line ARVs decrease. This shows how much ARV drug prices – and countries' relative use of cheap generic versus more expensive innovator drugs – impact future ARV therapy costs. Efforts to improve the quality of ARV therapy - in particular retention of patients on first-line regimens - will be important investments to maintain or reduce future costs.

38. The projected Global Fund share of these costs (Figure 6) reflects the assumption that contributions from other donors and domestic funding would over time stay the same (for the 2011 cohort). For ARV therapy and support to orphans and other vulnerable children, the decisions about future funding by the U.S. Global Health Initiative and the President's Emergency Plan for AIDS Relief (PEPFAR) [11, 12] will therefore have a major impact on the cost to the Global Fund.

39. For long-lasting insecticidal nets, the estimated Global Fund cost share was considerably higher (74 percent) than for ARV therapy (27 percent) and support to orphans and other vulnerable children (16 percent). This is consistent with the Global Fund's larger share of the overall international funding for malaria (49 to 68 percent between 2007 and 2009 [13]) compared to HIV/AIDS (20 percent in 2008 [14]).

40. As contributions from other sources throughout the coming 10 years are unsure, the actual future costs to the Global Fund may in reality lie anywhere between the presented cost share (Figure 6) and the full program-level estimated cost.

41. HIV/AIDS resource needs have been estimated by UNAIDS [15], the AIDS2031 initiative [16] and the Unified Health Millennium Development Goal costing model [17, 18] at between US$ 19 and US$ 49 billion per year. In comparison, the Global Fund's projected costs for ARV therapy and support to orphans and other vulnerable children represent relatively small amounts. Similarly, for long-lasting insecticidal nets, projected annual costs represent a small portion of the annual US$ 5.1 billion overall resource needs (according to Roll Back Malaria's Global Malaria Action Plan [19]). This illustrates that costing by individual service delivery areas should not be confused with estimating overall resource needs.

42. Especially for ARV therapy, service cost cannot be seen in isolation, as ARV therapy delivery depends critically on the concurrent implementation of other, supporting activities such as program management and training, and health systems strengthening in general. In Global Fund HIV/AIDS grants, activities aimed at creating a supportive environment and health systems strengthening are the second- and third-largest expenditure components after treatment.

Health Impact and Cost-Effectiveness

43. ARV therapy was estimated to save 2.0 million life-years on average annually between 2011 and 2020, and long-lasting insecticidal nets 6.2 million life-years annually. These estimates may be conservative, as they were based exclusively on mortality effects, ignoring morbidity effects, and for long-lasting insecticidal nets any health effect beyond children under five in sub-Saharan Africa.

44. For a lower cost, long-lasting insecticidal nets saved more life-years than ARV therapy, reflecting: (1) the young age that malaria deaths occur relative to HIV/AIDS deaths; (2) the general amplified impact of preventive interventions relative to curative interventions.

Limitations

45. These projections are indicative, given limitations associated with underlying assumptions, for which the existing evidence base was sometimes scarce.

46. On the cost side, service unit costs assumptions were based on the best available data from multiple sources, but the future development of these costs is uncertain. Unit costs may go down as maturing programs achieve economies of scale and improve their technical efficiency. Or they may go up as a result of diseconomies of scale and more expensive activities needed to reach out to the most-hard-to reach groups.

47. Especially for ARV therapy, costs per patient are imperfectly known. The assumptions included country-specific ARV prices, but these were assumed to stay fixed over the projection period. It is difficult to predict how actual ARV costs will develop over time, as these depend on both ARV prices and on the distributions of patients over available (first-line and second-line) regimens. For other cost drivers of ARV therapy, limited or no cost data is available from most countries [20], and the same fixed laboratory cost for all patients in all countries in all years was assumed, and regional averages of service delivery/health staff cost.

48. Both the cost and the health impact of ARV therapy depend on the assumed retention rates of patients on first-line regimens, for which available data are limited to the 22 countries covered in a recent WHO survey. With important variations in reported patient retention among countries, the actual retention rates are not precisely known (see Annex, section A).

49. The overall cost of comprehensive support for orphans and other vulnerable children in African settings with high prevalence of HIV has been carefully quantified (see Annex, section E), but there are large variations between support centers in actual level of support, and the typical Global Fund contribution – even if a country's entire support program is supported by a Global Fund grant – appears to be much lower than comprehensive support would cost.

50. Long-lasting insecticidal net impact projections depend critically on the actual long-lasting insecticidal net coverage (i.e. household ownership and usage by children under five) that long-lasting insecticidal net distributions achieve. Fixed relationships between reported long-lasting insecticidal net distributions and household coverage were assumed, and between household coverage and the mortality effect on children, based on a meta-analysis of cluster-randomized trials in six malaria-endemic African sites which had achieved high insecticide-treated net ownership (near-universal) and child usage (50 to 70 percent of children sleeping under a net any night). In real program settings where insecticide-treated net coverage is currently still lower than in the efficacy trials, however, these relationships may be different.

51. In conclusion, maintaining support for end-2011 cohorts of recipients should be affordable to the Global Fund and its international and country partners. The cost specific to the Global Fund will critically depend on contributions by other donors and from country domestic resources. In all cases, management of service delivery unit costs and seeking value for money and locally efficient service delivery systems in program implementation will be critical in order to contain costs.

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ANNEX

Modeling ARV therapy and orphan and other vulnerable children cohort behavior and unit costs, and ARV therapy and long-lasting insecticidal net health impacts

A. ARV therapy patient cohorts

For a cohort of HIV-infected patients starting ARV therapy in a given year, the number of patients surviving in each future year is determined from the number of patients in the previous year and the survival to the following year. Survival in the first year is assumed on treatment of 79.5 percent and in subsequent years of 95.8 percent, for all countries. These assumptions are based on retention rates reported by 38 National AIDS Programs to WHO in 2008 (Table A1) [21], weighted by the regional sample sizes in the WHO survey.

In this weighting, the survival assumptions are more optimistic than if weighted according to the Global Fund's regional distribution of ARV therapy patients, which are more concentrated in Africa (and less in Latin America and Caribbean), where retention rates are lower. The weighing by WHO sample size was chosen to reflect the expectation that over the coming years as ARV therapy programs in Africa mature and scale up, retention rates in African programs will improve and reach the levels currently achieved in later-phase programs in Latin America and Caribbean. This assumption is consistent with interpretation and assumptions in UNAIDS and WHO impact projections.

Table A1. Retention on ARV therapy as reported by National AIDS Programs, 2008 WHO survey

	12 months	24 months (cumulative)	36 months (cumulative)	48 months (cumulative)	Aggregate annual survival after first year
East, South and South-East Asia	80.2%	68.7%	66.7%	55.4%	88.3%
Europe and Central Asia	74.1%	63.4%	63.4%	66.8%	93.8%
Latin America and Caribbean	85.5%	78.6%	77%	74.5%	94.2%
Middle East and North Africa	89.6%	92.3%	86.8%	78.4%	98.9%
Sub-Saharan Africa	75.2%	66.8%	65.6%	67.2%	91.7%
Total – weighed by survey sample size	**79.5%**	74.8%	73.8%	73.1%	**95.8%**
Total – weighed by Global Fund distribution of ARV therapy patients	76.5%	88.6%	98.0%	99.1%	91.4%

A1. Migration from first-line to second-line ARV therapy

The number of patients on second-line regimens is calculated as the number on second-line in the previous year surviving to the current year (95.8 percent, Table A1) plus the number migrating from first-line to second-line in the past year. Migration rates were estimated by WHO based on data reported by 38 National AIDS Programs in 2008 (WHO unpublished meta-analysis). For countries without routine viral load monitoring, which included all the Global Fund-supported countries, annual migration was **2.6 percent** in sub-Saharan Africa and Latin America and Caribbean, and 1.1 percent in Asia.

For the start year of projections (2009) country-specific proportions of patients on second-line regimens were taken from the WHO 2008 survey for the 38 National AIDS Programs. For countries not participating in this survey, regional average rates were applied. Across all Global Fund supported countries, the weighted average proportion was 2.5 percent of patients on second-line regimens in 2009.

B. ARV therapy cost per patient-year: laboratory and service delivery components

Annual laboratory costs are calculated as the median of 12 published studies (Table A2). Service delivery costs are calculated from the number of outpatient visits and inpatient days per person per year. The median values from the studies shown in Table A3 were used.

Table A2. Laboratory costs of ARV therapy, US$ per patient-year

Country	Comments	Cost	Source
Côte d'Ivoire	CD4 cell count every six months at US$ 25, plus US$ 7.91 for initiation of ARV, averaged over four years	52	[22]
Ethiopia		207	[23]
Mexico	ARV = average of first, second and third year; Opportunistic infections =-1 yr for OPD, IPD, Avg of all yrs for OI drug costs	366	[24]
Nigeria	Assume monthly visits for ARV patients	204	[25]
Thailand	ALL MODEL ASSUMPTIONS: ARV patients have monthly OPV, lab tests 4x/yr, AIDS patients without ARV average length of stay=6.4 & average hospital admissions=3	459	[26]
Uganda	12 ARV visits per year - no costing of IPD; Table 11 shows staff requirements if ARV visits separate from OI etc - ratio used to calculate OI OPD	74	[27]
Zambia	1 session to initiate ARV, 4 sessions per year to monitor	178	[28]
South Africa	Actual tests in patient pop: 1.8 CD4 Count tests/yr (at R60/test), 1.6 Viral Load count tests/yr (at R300/test), 5 ALT (R36), 5 FBC (R46), and 2 chemistry (R24-53), converted to USD (2004 rate R 6.46) (Lab tests 13% of total costs)	156	Long L, Rosen S, Meyer-Rath G. Costing Treatment by the Guidelines: Using the 2004 South Africa National Guidelines to Estimate the Cost of Adult Antiretroviral Therapy. March 2009. internal PP
Brazil	Reports that Brazilian Health Ministry intends to do 400,000 tests at $18 million, assuming 4 tests/yr	180	[29]
Caribbean	Estimates $400,000/1000persons/yr for 2 CD4 and viral load tests	400	[30]
Haiti	Total reported is $130.00 for a mean number of 11.3 ART monitoring lab tests; 1.3 CD4 cell counts and 0.4 chest radiographs (Table 2) per 299 days of treatment. Scaled up to 365 days of treatment brings cost to $158.70. (Lab tests comprised 15% of total costs.)	159	Koenig S, Leger P, Severe P, et al. Cost of HIV/AIDS treatment during the first year after ART initiation in Port-au-Prince, Haiti. AIDS 2006 - XVI International AIDS Conference, 2006. Abstract no. CDB0547 / [31]
South Africa	Total reported is $272/6 mo and included drug toxicity and clinical efficacy assessments - weekly for first 4 weeks and monthly thereafter; CD4 and viral load tests - at baseline and every 2 months; and HIV genotypic resistance - at baseline and at 6 months (Lab costs 21% of 6-mo total $1286)	544	[32]

Country	Comments	Cost	Source
South Africa (KwaZulu-Natal)	Total lab cost is per patient year. No details on what tests are included. Total average costs were R 6848, with breakdowns: personnel R1927, lab R1514 (US$223.63), equipment R44, supplies R90, drugs R3208, utilities R62. Converted to USD (2006 rate R 6.77) (Lab costs were 22%of total.)	224	Silvestri A, Marra C, Vella V. Evaluation of Antiretroviral therapy (ART) in the public sector delivery sites of KwaZulu-Natal (KZN), 2004-06. internal PP
Rwanda	Monitoring laboratory tests per patient per year (55/yr), CD4 tests, 2 per year (10.52/ea) Table 2 contains testing pricing.	66	[33]
South Africa	Reports unit costs in USD for CD4 cell count ($9.32), HIV RNA load ($42.62) and alanine transaminase ($4.76). Also reports cost per PY in program ($92.26) at end of year one.	92	[34]
Median		**180**	

Table A3. Service delivery costs of ARV therapy, per patient-year

Country	Comments	Out-Patient Visits	In-Patient Days	Source
Ethiopia		9		[23]
Mexico	ARV=Avg of 1st, 2nd and 3rd yr; OI=-1 yr for OPD, IPD, Avg of all yrs for OI drug costs	10	12.17	[35]
Nigeria	Assume monthly visits for ARV patients	12		[25]
South Africa	ARV=Avg of 1st yr, 2nd yr, 3 yr, >3 yr; OI =Avg of CD4<50, CD4 50-199. (Deleted lab costs on 11/30/09 b/c they estimate protocol, not actual.)	5.62	0.45	[36]
South Africa	Averaged Non-AIDS/AIDS usage for HAART/No-ART patients; didn't split drug costs out from svc delivery for OI tx	8.17	1.56	[37]
Thailand	ALL MODEL ASSUMPTIONS: ARV patients have monthly OPV, lab tests 4x/yr, AIDS patients without ARV average length of stay=6.4 & average hospital admissions=3	12	Assumes 40% in IPD due to ART	[26]
Uganda	12 ARV visits per year - no costing of IPD; Table 11 shows staff requirements if ARV visits separate from OI etc - ratio used to calculate OI OPD	12		[27]
Zambia	1 session to initiate ARV, 4 sessions per year to monitor	4		[28]
Median		**9.5**	**1.56**	

C. Cost of end-of-life care of ARV therapy patients

The cost of end-of-life care for HIV patients once they fail ARV therapy was estimated based on literature review of non-ARV therapy treatment use and costs. An average of US$ 50 worth of drugs was consumed over a patient's lifetime, and usage of health care averaged 9.7 inpatient days and 5.5 outpatient visits per patient-lifetime.

Using CHOICE cost estimates of inpatient days and outpatient visits gives service delivery costs of US$ 145 to US$ 800, depending on the region. The average lifetime cost of drugs plus service delivery was approximately US$ 480 per patient. It was assumed that these costs cover a period of about 1 ½ years, one year before ARV therapy eligibility and half a year after. For people already on ARV therapy, only the half year of treatment of opportunistic infections during the final stages of life was considered. The cost assumption for end-of-life care after ARV therapy was therefore US$ 160.

D. Health impact

D1. ARV therapy: health impact

ARV therapy impact projections assume that all ARV therapy is provided to HIV-positive people in need of such treatment, which is operationalized as a median of three years before estimated time of AIDS-related deaths [2, 38]. Survival on ARV therapy is calculated as specified above.

If ARV therapy is stopped or patients in need cannot access ARV therapy, most patients will die quickly. The cumulative mortality rates estimated for people in need of ARV therapy but never on treatment were applied to calculate this mortality. These rates are based on analyses of time from infection to AIDS deaths conducted by the ALPHA network, a collaboration of cohort studies in Africa [39, 40] and of time from infection to ARV therapy eligibility [41]. From these data Weibull survival curves were calculated for progression from ARV therapy eligibility to AIDS death in the absence of treatment (Table A4).

Using these cumulative mortality rates, the number of people from each patient cohort that would still be alive over subsequent calendar years was calculated and compared to numbers still alive and on ARV therapy, to estimate numbers of deaths averted and life-years saved in each calendar year.

Table A4. (Cumulative) percentage of patients who have died, in years since eligibility for ARV therapy

	Male	Female
Year 1	20.7	16.2
Year 2	50.1	41.2
Year 3	68.6	58.7
Year 4	80.3	71
Year 5	87.6	79.7
Year 6	92.2	85.7
Year 7	95.1	90
Year 8	96.9	93
Year 9	98.1	95.1
Year 10	98.8	96.5

D2. Long-lasting insecticidal nets: health impact
Long-lasting insecticidal nets were assumed to avert mortality in children under five in sub-Saharan Africa.

The number of **insecticide-treated nets available** *per person at risk of malaria* in each country was calculated as the number of insecticide-treated nets distributed in the past three years (Table 1) divided by the country population at risk of *Plasmodium falciparum* malaria [42]. Population sizes were derived from UN Population Division Projections for 2006 to 2015 [43]. For 2016-2020, populations were assumed to grow at the same average rate as in 2011-2015.

Proportions of households owning at least one net were derived from the number of nets per person at risk [44], as:

$$Y = 1.8199 * X$$

where: X = proportion of household with at least one net;
Y = the number of nets available per person at risk;
And 1.8199 based on [44].

Country estimates of **malaria deaths in 2006** in each country were used [45] to estimate the number of deaths that would have occurred if there had not been any insecticide-treated nets in 2006, as follows:

$$D_0 = D_{2006}/((1-X_{2006}) + X_{2006}*E)$$

Where:
- D_0 = deaths due to malaria in 2006 if no insecticide-treated nets in a country
- D_{2006} = actual malaria deaths estimated for 2006
- X = percentage of households owning at least one insecticide-treated net, as derived from a dynamic model of insecticide-treated net supply, distribution and coverage [46]
- E = effectiveness of owning at least one net in reducing malaria-attributable mortality in children under five: assumed to be **55** percent based on a meta-analysis community-randomized trials in stable endemic African settings [47].

Numbers of malaria deaths for years 2007 to 2020 in the counterfactual scenario without insecticide-treated nets were derived from the corresponding 2006 estimates, assuming annual increase according to the annual rate of population growth.

The **number of malaria deaths averted** in each year was derived from the proportion of households with at least one insecticide-treated net, as below:

$$V = D_i * X_i * e$$

Where :
- V_i = Deaths averted in year i
- Di = Deaths due to malaria in year i if no insecticide-treated nets in a country
- X_i = Percentage of household owning at least one net in year i
- E = effectiveness of owning at least one net in reducing malaria-attributable mortality in children under five.

This assumes that children living in households owning nets have the same risk of dying from malaria as children in households not owning nets.

Deaths averted were translated into **life-years saved**, assuming a median age at death from malaria of 1.8 years [10], subtracted from the life expectancy at birth for each country [48]. Life-years saved are attributed to the calendar year of the death averted. A 3 percent annual discounting was applied to discount the value of benefits expected in the future. As a result, for a median estimated life expectancy from the age of (averted) malaria death of 50 years, the discounted life-years saved per death averted is 25 years. In contrast to discounting for future life-years associated with each death, (as for ARV therapy) no discounting is applied between subsequent years of deaths averted.

D3. Limitations in long-lasting insecticidal net health impact estimation

Assumptions that may lead to an under-estimation of malaria deaths averted:

- Assumed three-year long-lasting insecticidal net life-span: If long-lasting insecticidal net last four years or more, the potential coverage and number of deaths averted may be higher.
- The estimate of insecticide-treated net effectiveness is derived from randomized control trials and the effectiveness in real life may be more extensive, especially if combined with other interventions.

Assumptions that may lead to an over-estimation of malaria deaths averted:

- The number of household owning at least one net may be an overestimate if, as net coverage expands, more nets are acquired by households already owning a net rather than being distributed to households without a net.
- Long-term trends for an improvement in living standards and a gradual decrease in risk of dying from malaria.
- Likely long-term improvements in the health status of child populations (owing to increase in birth intervals, improved nutrition etc.) could lead to a reduction in the baseline number of deaths without malaria specific interventions.
- The estimate of insecticide-treated net effectiveness is derived from randomized control trials and the effectiveness in real life may be more limited.
- Nets may be preferentially distributed to households with lower prior risks of malaria.
- The number of life-years gained may be overrepresented if a child's death has been averted on more than one occasion.

Assumptions for which there is limited evidence, but the direction of bias is uncertain:

- Changes in demographic structure of populations (such as reduction in birth rates, increase in numbers of women of reproductive age).
- The estimate of insecticide-treated net effectiveness is derived from a only a limited number of randomized control trials (four trials in three countries).

E. Support to orphans and other vulnerable children

E1. Cohort behavior

The Spectrum projection package was used to estimate the total number of orphans in 2009 (AIDS and non-AIDS, single and double) by single age [2]. The age distribution of orphans varies by country depending on trends in fertility, non-AIDS mortality and HIV. Country-specific age distributions were used to project proportions of orphans and other vulnerable children from each cohort (2009, 2010, 2011 etc.) that are still under the age of 18 in each future year.

Some children will die each year. Age-specific mortality rates for all children under the age of 18 were calculated for the ten countries with largest number of Global Fund-supported orphans (eight of which are in Africa). Across those countries, average annual mortality was 0.026 for children aged 0 to 4, 0.0038 for those between 5 and 9, 0.0025 for ages 10 to 14 and 0.0026 for ages 15 to 19, with a weighted average mortality rate for all orphans and other vulnerable children (0 to 17) of 0.0050 per year. These average annual mortality rates were used to calculate survival. These rates reflect current country-wide survival rates, although, with comprehensive support ensuring adequate food, health care and sanitation, lower mortality rates among the supported orphans and other vulnerable children could be expected.

Health impact was not estimated due to limited empirical data.

E2. Support cost

The cost of support to orphans and vulnerable children varies widely by the number and type of services provided and by the mechanism of support. Comprehensive support includes food, clothes, shoes, bedding, health care, education, training, and psychosocial support. Most programs provide only some of these services, but some children access support from more than one program. From data collections across 300 nongovernmental organizations and 7,400 sites providing support in sub-Saharan Africa, the average cost across all services has been estimated at US$ 652 per child per year [3]. This study also estimated that costs would decline to US$ 224 per child-year with economies of scale, as programs scale up to national level. The amount of US$ 224 was used in the resource need projections.

In comparison, for an alternative approach to providing support (via cash grants to families or communities, as used in a few countries including South Africa) monthly costs may be as low as US$ 10, but this reflects less comprehensive support.

Global Fund-supported services are concentrated in the same countries as Global Fund-supported ARV therapy: 14 countries together cover the top ten of Global Fund-supported ARV therapy and the top ten of Global Fund-supported services for orphans and other vulnerable children (some countries are in both categories). These 14 countries together cover 69 percent of Global Fund-supported ARV therapy patients and 94 percent of Global Fund-supported services for orphans and other vulnerable children.

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