Cost and Cost-Effectiveness of Switching From d4T or AZT to a TDF-Based First-Line Regimen in a Resource-Limited Setting in Rural Lesotho

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Background: Latest World Health Organization guidelines recommend shifting away from Stavudine (d4T)-based regimens due to severe side effects. However, widespread replacement of d4T by Tenofovir (TDF) or Zidovudine (AZT) is hampered by cost concerns.

Methods: We established the cost-effectiveness of alternative first-line regimens using primary utilization, cost, and outcome data from a program in a rural district in Lesotho. We calculated cost per patient-year, incremental costs, and incremental cost-effectiveness ratios per life year, and per Quality Adjusted Life Year gained. Uncertainty was assessed using multiway and probabilistic sensitivity analyses.

Results: Our study included 1260 patients representing 1635 patient-years on antiretroviral therapy (ART). Six hundred eight patients were on TDF, 290 were on AZT, and 362 were on d4T. Patients on d4T experienced more toxicities; toxicities with the biggest impact on quality of life were moderate neuropathy and severe lipodystrophy. The cost per patient-year ranged from US $266 on d4T to US $353 on TDF. Inpatient care and essential drug costs were higher for patients on d4T than on AZT or TDF. Incremental cost-effectiveness ratio results suggest that AZT-based ART is weakly dominated by a combination of d4T- and TDF-based ART.

Discussion: This is one of the first analyses to investigate the cost-effectiveness of TDF using primary data in a resource-poor setting. Although TDF-based first-line ART is more costly than d4T, it is also more effective. Political pressure should be exerted to encourage further price reductions and additional generic manufacturing for TDF and partner drugs such as Efavirenz. This should be met by a commitment from donors and implementers to ensure that supply is met by a clear demand.

Key Words: cost-effectiveness, Tenofovir, Stavudine, toxicity

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INTRODUCTION

The latest World Health Organization guidelines for antiretroviral therapy in resource-limited settings released in 2009 recommend a shift away from Stavudine (d4T)-based first-line regimens due to the severe, sometimes life-threatening side effects associated with this drug.[1] The use of d4T in Western settings began to decline as early as 2000, and current guidance in Europe states that d4T should only be used as a last resort.[2] Zidovudine (AZT) has been recommended by World Health Organization guidelines since 2002. The potential role of Tenofovir (TDF) in first-line has been acknowledged since 2003, although limited availability and high cost were acknowledged as constraints. TDF was finally recommended as a first-line option in 2006.[3] An additional advantage of TDF is its availability as a once-daily regimen, which is supportive of improved adherence.[4]

Despite these advantages, the widespread replacement of d4T by TDF or AZT is hampered by cost considerations: d4T remains the cheapest of the 3 drugs, in terms of cost per daily dose, and major donors continue to resist supporting the full elimination of d4T. As of July 2010, 14 of 52 developing countries surveyed by World Health Organization had yet to start phasing out from d4T to TDF or AZT.[5]

Modeled cost-effectiveness analyses have suggested that, once related costs such as laboratory monitoring requirements and side-effect management are taken into account, the cost-effectiveness of TDF would be more favorable. In India, TDF was found to be more cost-effective than d4T (ie, same overall costs, but higher outcomes).[6] Another modeled study based in South Africa indicated that the price of TDF would need to fall from US $17 to US $6.17 per month for TDF to have the same overall cost as d4T-based

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antiretroviral therapy (ART).[7] However, cost-effectiveness estimates using primary cost and outcome data from routine programs are lacking.

The aim of this study was to assess the cost-effectiveness of TDF versus AZT- and d4T-based first-line regimens from the health system's perspective based on primary patient-level data collected within an observational cohort in rural Lesotho.

METHODS

Study Setting and Treatment Strategies

All data included in this study were collected in Lesotho, a poorly resourced country landlocked by South Africa, with the third highest HIV prevalence in the world (23% general adult prevalence). In 2006, Médecins Sans Frontières and the Ministry of Health and Social Welfare established a primary care HIV/AIDS care and treatment program in the Scott Catchment Area (population 200,000). ART services began in March 2006, and by the beginning of 2010 the program had enrolled 6081 patients on ART. Treatment is provided across 14 primary health care centers and 1 district hospital.[8]

When ART was initiated in Scott district, the standard first-line treatment included either d4T or AZT for pregnant women as the nucleoside reverse transcriptase inhibitor (NRTI) together with Lamivudine (3TC) as the second NRTI and either Nevirapine (NVP) or Efavirenz (EFV) as the non-NRTI. Due to the high rate of tuberculosis (TB) coinfection, EFV is more commonly prescribed than NVP, except for women of childbearing age who are not using contraception or are in the first trimester of pregnancy. In late 2007, the Ministry of Health and Social Welfare of Lesotho introduced TDF as an alternative to d4T or AZT in the first-line regimen. Implementation of the new guideline followed a phased approach, resulting in the concurrent use of all 3 first-line NRTIs during 2008. AZT was still chosen as the NRTI of choice for pregnant women and TDF was prescribed in combination with EFV to enable a once-daily regimen.

As it is not possible to treat a whole population with a single first-line regimen due to various exclusion criteria, this analysis evaluates the cost-effectiveness of 3 possible first-line prescribing options. Option I is a d4T-based regimen (with an alternative of AZT for women who became pregnant); option II is an AZT-based regimen (with TDF for patients with hemoglobin [Hb] <8 g/dL and d4T for those with creatinine clearance <50 ml/min); option III is a TDF-based regimen (with AZT for pregnant women and/or those with creatinine clearance <50 ml/min and d4T Hb <8 g/dL). In this article, when we refer to d4T, AZT, or TDF, it refers to the results for patients who are receiving 1 of these drugs. On the other hand, when we refer to, for example, a d4T-based first-line regimen, then it implies that patients will be predominantly on d4T-based ART, but alternative regimens will be prescribed for patients with exclusions for d4T.

Study Design

This study established the cost-effectiveness of alternative first-line regimens from the health system perspective using primary resource utilization, cost, and outcome data. The study cohort included all patients starting on ART during 2008, with follow-up until the end of 2009. Both costs and outcomes are expressed per patient-year on ART.

Costs, calculated from the health system's perspective, include antiretrovirals (ARVs), other essential medicines, inpatient care, laboratory investigations, counseling, cotrimoxazole prophylaxis, and nurse consultations. Costs are expressed in 2009 prices converted to US $ according to the exchange rate at that time (US $ 1 = 9.76 maloti; http://www.xe.com/ucc/, accessed 01 December 2009). Outcomes are expressed as life years and Quality Adjusted Life Years (QALYs). Key results include the cost per patient-year, outcomes per patient-year, incremental costs, and incremental cost-effectiveness ratios (ICER). The ICER for the most effective/costly option is calculated as the ratio of the incremental costs of this option versus less costly options divided by the associated incremental outcomes. If one option has a higher ICER than a more effective strategy, it is said to be weakly dominated by a combination of the remaining 2 strategies.[9] Given that the analysis was restricted to a 1-year period, discounting was not undertaken.

Given that the analysis was based on routine clinical data, ethical review and individual patient consent were not sought. All patient information was entered into a database using coded identification numbers, and no information that could reveal patient identity was collected.

Cost per Patient-Year

Cost results are expressed as the cost per patient-year by drug (ie, d4T, AZT, TDF), and within each of the first-line ART options (ie, d4T-based ART, AZT-based ART, and TDF-based ART). These were calculated by multiplying the utilization of a full range of HIV-related services with the associated unit costs.

Utilization estimates included nurse and counselor consultations, inpatient days, laboratory tests (CD4 counts, alanine aminotransferase, creatinine, Hb and sputum smear for TB), essential drugs including cotrimoxazole prophylaxis, and ARVs (including d4T, AZT, TDF, 3TC, EFV, and NVP depending on the first-line regimen). These utilization estimates were extracted from clinic files by a clinician and a researcher with experience in cost analysis; all hospitalizations documented from the clinic were cross-checked against hospital admission notes. Utilization estimates are expressed as the mean (with 95% confidence or uncertainty intervals) per patient-year, by drug.

A nonpatient-specific unit cost per consultation or per inpatient day was then established (this is the unit cost stripped of any items that could be directly attributed to patients, including all medicines and laboratory investigations). The cost per nurse and counselor consultation was calculated using routine accounting information from 6 ART clinics based in 1 hospital outpatient department and 5 primary care facilities. Costs included the full cost of employment of nurses and a share of facility running costs (administrative staff, transport, and other overheads). The cost per nurse or counselor consultation was estimated by dividing these total costs by the total number of visits during the same period. Similarly, the cost per inpatient day at the hospital included the cost of employment of all staff and hospital running costs, split equally between inpatients.[9]

The patient-specific items that were stripped from consultation and inpatient costs were estimated by establishing the medicine costs associated with treating the most common side effects and HIV-related infections and events. Side effects include neuropathy, lipodystrophy, rashes, lactic acidosis, anemia, and renal toxicity, whereas HIV-related infections include cryptococcal meningitis, diarrhea, oral or genital herpes, oral or esophageal candida, pneumocystis carinii pneumonia, rashes, respiratory tract infections, TB, and toxoplasmosis. Medicine costs were calculated by establishing a standard protocol of medicines to treat the identified side effects and HIV-related infections. The cost per patient-year of each medicine protocol was then established by multiplying the incidence of each side effect or infection by the medicine cost of treatment.

ARV costs were based on actual prices obtained from the Clinton Foundation during 2009. The cost per laboratory investigation included reagents and consumables, a share of the cost of employment of laboratory staff, running costs, and the cost of specimen collection. Finally, costs associated with training, supervision, and clinical mentorship included the cost of employment of a doctor, nurse and the associated transport costs. These were split equally between all patients on ART to calculate a cost per patient-year. Additional details are available in Supplemental Digital Content 1 (http://links.lww.com/QAI/A197).

Outcomes per Patient-Year

Outcomes include life years and QALYs. Mortality out-of-facility was reported to clinic staff by relatives, village leaders, community health workers, and facility TB/HIV lay counselors who undertake defaulter tracing. Defaulter tracing is done within a few days of a patient missing an appointment such that early mortality among those lost to follow-up is documented within a month of a missed appointment. Kaplan–Meier estimates were used to calculate rates of death and defaulting stratified by drug and time on ART (0–3, 3–6 months, and 6–12 months). Patients were censored when they were transferred to another ART program or at the end of 2009.

We developed a visual analog scale to assess decrements in health-related quality of life (HRQoL) associated with the common adverse events related to d4T, AZT, and TDF. This scale, which was developed by clinical staff and revised after piloting, included the following side effects: anemia (Hb $<$ 8 g/dL); severe neuropathy (symptoms not controlled by analgesia and requiring a switch in ARV); moderate neuropathy (symptoms controlled through daily analgesia); mild neuropathy (slight pins and needles in hands and feet); severe lipodystrophy (patient feels very stigmatized by appearance requiring a switch in ARV), mild lipodystrophy (patient not affected by appearance); severe lactic acidosis (patient has abdominal pain, vomiting, and breathlessness requiring a switch in ARVs); mild lactic acidosis (slight abdominal pain and possible slight weight loss); and renal toxicity (creatinine clearance between 30 and 50). In the scale, a 0 value is equivalent to death whereas a value of 1 is equivalent to perfect health. The resulting median HRQoL weight was used to estimate QALYs by applying this decrement over the duration of each of the adverse events encountered in our sample of patients. A value of 1 was applied to periods where there were no toxicities, and a 0 value was applied to patients who had died or were lost to follow-up from the time that these events were recorded.

Uncertainty and Sensitivity Analyses

There are 3 sources of uncertainty that are relevant to this study: the data set, generalizability of results, and the choice of analytical methods (eg, valuation of outcomes).[10] Uncertainty relating to the data has been assessed using probabilistic sensitivity analysis. Where possible, distributions (uncertainty intervals) were specified on utilization, incidence, and outcome variables, and uncertainty was captured by running 100,000 second-order Monte Carlo simulations. During each simulation, a different value is sampled from within each uncertainty interval. When a number of simulations are run, parameter uncertainty is captured as uncertainty intervals around overall costs, outcomes, and ICERs. To assess uncertainty in our choice of analytical methods, we have expressed outcomes as both life years and as QALYs. We have not assessed uncertainty associated with discounting as the time horizon of this study precluded any need for discounting. Finally, we have sought to strengthen the generalizability of our results through additional multiway simple sensitivity analyses. First, we have run a scenario where EFV is substituted for NVP. Second, we have run a scenario varying the costs of treating toxicities and HIV-related infections. These scenarios increase the generalizability of our results (1) to settings where EFV is routinely prescribed instead of NVP within first-line regimens and (2) to settings where access to inpatient care and where the medicine costs of treating toxicities and HIV-related infections might differ from rural Lesotho. All sensitivity analyses were run in TreeAge Pro 2006.

RESULTS

Our study included 1260 patients representing 1635 patient-years on ART. Six hundred eight patients were on TDF, 290 were on AZT, and 362 were on d4T. Median CD4 at treatment initiation was 215 cells/mm^3 (interquartile ratio 125–289) and two thirds (66%) of patients were women. Median time on ART was 508 days. Patient characteristics according to treatment regimen at initiation are shown in Table 1.

The unit costs of the key resources used to manage a patient on ART and the utilization of these services/resources are summarized in Table 2. The latter in addition contains the uncertainty intervals around the mean estimates per patient-year that are used within the probabilistic sensitivity analysis. There were no significant differences in consultations and inpatient days between regimens, and similar quantities of laboratory investigations were also performed. There was, however, a key difference in terms of the proportion of patients prescribed EFV together with TDF (99.8% versus 41.1% and 48.2% in d4T and AZT, respectively). Given that EFV costs more than NVP, the higher utilization of this drug will have implications for the overall incremental cost of the TDF regimen relative to d4T and AZT. In addition, Table 2 gives a breakdown of the cost per patient-year, by ARV, ranging from US $266 on d4T to US $353 on TDF. The highest share of costs was for ARVs, followed by

TABLE 1. Characteristics of Patients According to Treatment Regimen at Initiation

	Total (N = 1260)	d4T (N = 362)	AZT (N = 290)	TDF (N = 608)
CD4 (median, IQR)	214.5 (125–289)	195 (104–279.5)	240 (157–310)	213 (119–283)
Age (median, IQR), years	38 (29–48)	39 (28–50)	33 (26–45)	29 (32–48)
Women, N (%)	831 (66.0)	264 (72.9)	247 (85.2)	320 (52.6)
Follow-up (days) (median, IQR)	508 (398–608)	547 (410–635)	518 (378–587)	494 (400–595)
TB, N (%)	216 (17.1)	62 (17.1)	38 (13.1)	116 (19.1)

IQR, interquartile ratio.

counseling and supervision costs. Inpatient care and essential drug costs were higher for patients on d4T than on AZT or TDF.

Supplemental Digital Content 2 (http://links.lww.com/QAI/A198) summarizes the costs of essential drugs needed to manage key side effects and HIV-related infections. The cost differs depending on whether the episode is managed on an outpatient or an inpatient basis. These, together with the incidence of these events per patient-year, give a mean cost per patient-year in each regimen. Although the highest costs per patient-year were for patients receiving d4T, in general these costs were very low.

As expected, patients on d4T experienced significantly more toxicities than the patients on the other ARVs (see **Supplemental Digital Content 3,** http://links.lww.com/QAI/A199). Results from the visual analog scale suggest that the lowest HRQoL was associated with severe lactic acidosis. However, the impact of toxicity on overall HRQoL will depend on the amount of time for which it is experienced. The annual HRQoL weight takes this duration into account by assuming that the patient is returned to perfect health once the toxicity has been resolved. This calculation indicates that the toxicities with the biggest impact on annual HRQoL are moderate neuropathy and severe lipodystrophy.

Table 3 summarizes the cost per patient-year, outcomes, and ICERs by first-line option. Because it is not possible to treat a whole population with a single regimen, these results reflect the distribution of patients between regimens based on the characteristics of the cohort. Results indicate that the

TABLE 2. Unit Costs (US $), Utilization per Patient-Year, and Cost per Patient-Year (US $) by ARV

					Cost per Patient-Year		
	Unit Cost/Price	d4T	AZT	TDF	d4T	AZT	TDF
Health services	Per unit		Utilization per patient-year		50.32	46.34	48.15
Inpatient days (mean, 95% UI)	43.32	0.33 (0.11–0.55)	0.23 (0.05–0.42)	0.28 (0.13–0.43)	14.30	10.11	12.13
Nurse consultations (mean, 95% UI)	2.96	12.17 (11.91–12.43)	12.24 (11.81–12.67)	12.17 (11.91–12.43)	36.02	36.23	36.02
Laboratory tests	Per unit		Utilization per patient-year		19.63	21.75	19.95
AFB (mean, 95% UI)	2.13	0.43 (0.35–0.52)	0.36 (0.27–0.45)	0.26 (0.21–0.31)	0.92	0.77	0.55
CD4 count (mean, 95% UI)	6.62	1.96 (1.89–2.04)	2.01 (1.92–2.09)	2.02 (1.97–2.07)	12.98	13.31	13.37
HB (mean, 95% UI)	2.32	1.10 (1.03–1.16)	2.05 (1.93–2.18)	1.01 (0.97–1.05)	2.55	4.76	2.34
ALT (mean, 95% UI)	1.01	1.89 (1.79–1.99)	1.75 (1.65–1.85)	1.46 (1.40–1.51)	1.91	1.77	1.47
Creatinine (mean, 95% UI)	1.19	1.05 (0.97–1.14)	0.98 (0.88–1.08)	1.86 (1.81–1.91)	1.25	1.17	2.21
Antiretrovirals	Per patient-year		Proportion per patient-year		75.79	146.24	177.69
TDF 3TC EFV	177.71	—	—	99.8%	—	—	177.35
TDF 3TC NVP	170.04	—	—	0.2%	—	—	0.34
AZT 3TC EFV	156.47	—	48.2%	—	—	75.42	—
AZT 3TC NVP	136.73	—	51.8%	—	—	70.83	—
d4T 3TC EFV	97.07	41.1%	—	—	39.90	—	—
d4T 3TC NVP	60.94	58.9%	—	—	35.89	—	—
Essential medicines	Per patient-year		Proportion per patient-year		10.89	7.69	6.86
Cotrimoxazole prophylaxis	5.75	100%	100%	100%	5.75	5.75	5.75
Essential medicines for HIV-related infections and toxicities	*	*	*	*	5.14	1.94	1.11
Program-level costs	Per patient-year		Proportion per patient-year		100.71	100.71	100.71
Supervision	85.95	100%	100%	100%	85.95	85.95	85.95
Counseling	14.76	100%	100%	100%	14.76	14.76	14.76
Total					257.34	322.73	353.37

*See Supplemental Digital Content 2 (http://links.lww.com/QAI/A198) for additional details.
UI, uncertainty interval; MSF, Médecins Sans Frontières; ALT, alanine aminotransferase.

TDF-based regimen was associated not only with the highest positive outcomes per patient-year but also with higher costs (as indicated by the uncertainty intervals around costs calculated using probabilistic sensitivity analysis). The ICER results suggest that the AZT-based regimen is weakly dominated by a combination of d4T- and TDF-based ART. The ICER for TDF was higher when outcomes were expressed as life years. This is because the QALY measure captures both length of life and the improved HRQoL associated with the lower incidence of toxicities in patients on TDF.

Results of the 2 multiway sensitivity analyses are presented in Figures 1 and 2. Although we varied the costs of inpatient care and essential medicines to treat toxicities and HIV-related infections over a wide range (from a 50% reduction in costs to a 200% increase), the percentage change in overall costs was small. In addition, because all first-line regimens make use of these resources (albeit to varying extents), any change in these items has a small impact on the relative cost-effectiveness of regimens. On the other hand, we ran a scenario where all patients were assumed to receive EFV instead of NVP. Because EFV is more costly than NVP, and because close to 100% of those on TDF receive EFV in comparison with 41% and 48% on d4T or AZT (Table 2), variations in the usage of EFV will have an impact on the incremental costs and cost-effectiveness of TDF relative to the other regimens. Under the baseline scenario, TDF-based ART costs US $84 more than d4T-based ART, whereas under the EFV scenario, the difference is US $66, which amounts to a 22% reduction in these cost differences.

DISCUSSION

In our routine program we found that TDF was associated with a lower rate of toxicity-driven regimen substitutions compared with AZT and d4T, an observation that is consistent with both trial data and evidence from routine programs.[11–13] TDF-based ART generated higher life years and QALYs than AZT- or d4T-based options.

Some caution is required in the interpretation of cost-effectiveness results. If the budget were to stay constant, our results suggest that health would be maximized through providing TDF-based ART concurrently with d4T-based ART within this rural Lesotho context. Anticipated price reductions in TDF would improve the cost-effectiveness of TDF-based ART, with the implication that a greater proportion of those in need would have access to this superior treatment. On the other hand, if the HIV-related budget can be increased, then the TDF ICER could be used by policymakers to judge the relative cost-effectiveness of TDF in comparison with other potential usages of these funds in first-line ART.

Our findings are not readily comparable with other estimates as there are few published studies in the current literature on the use of TDF in resource-poor settings. A cohort study from Zambia showed similar low rates of toxicity but no difference in outcomes, although it was noted that their TDF cohort started with more advanced disease and follow-up time was short. A cost analysis of switching from d4T to TDF in this program showed an average cost increase of between US $105 and US $206 per patient-year in care. Health-related quality of life and cost-effectiveness were not, however, presented.[14] In a recent report from Burma,[15] where TDF was introduced in a privately funded program, the annual cost of providing ART care with TDF was estimated at US $276 per patient per year with observed advantages of simplification in their service delivery. A study from Spain[16] comparing TDF/emtricitabine versus AZT/3TC using clinical data for both effectiveness and tolerability found that TDF/emtricitabine had a lower ICER than AZT/3TC. Other studies on cost-effectiveness of TDF have used models based on parameters drawn from the literature to estimate costs and outcomes.[6,7] One such study from South Africa estimated that the price of TDF would need to fall by 64% to achieve cost neutrality in comparison with d4T. However, this study included far higher unit costs (including TDF prices) and high levels of secondary care services that are not normally available in resource-poor settings.[7]

Strengths of our study include the fact that our costs are based on primary health care utilization, costing, and clinical event data from a routine program in a rural setting, and can thus be considered to provide a more accurate estimation of actual costs to providers in similarly resourced settings. There are several limitations inherent to observational studies. First, clinical events such as mortality, loss to follow-up, and toxicity could be subject to confounding. We did not adjust for confounders in our event rate allocation for this study, but in a separate multivariate analysis that assessed the hazard of

TABLE 3. Costs, Outcomes, and Incremental Cost-Effectiveness Ratios, by First-Line ART Option

	d4T Based	AZT Based	TDF Based
Composition of regimen	93% d4T	1% d4T	1% d4T
	3% AZT	96% AZT	22% AZT
	0% TDF	3% TDF	77% TDF
Cost per patient-year (mean, 95% UI)	261.92 (254.96–268.89)	323.07 (317.07–329.15)	345.42 (341.25–349.61)
Life years per patient-year (mean)	0.83	0.86	0.90
QALYs per patient-year (mean)	0.79	0.86	0.89
ICER* (life years) (mean, 95% UI)	N/A	Weakly dominated	1193 (1153–1233)
ICER (QALYs) (mean, 95% UI)	N/A	Weakly dominated	835 (807–863)

*The ICER summarizes the ratio of the difference in costs to the difference in outcomes after eliminating weakly dominated options. The latter occurs when an option has a higher ICER than a more effective strategy.
N/A, not available.

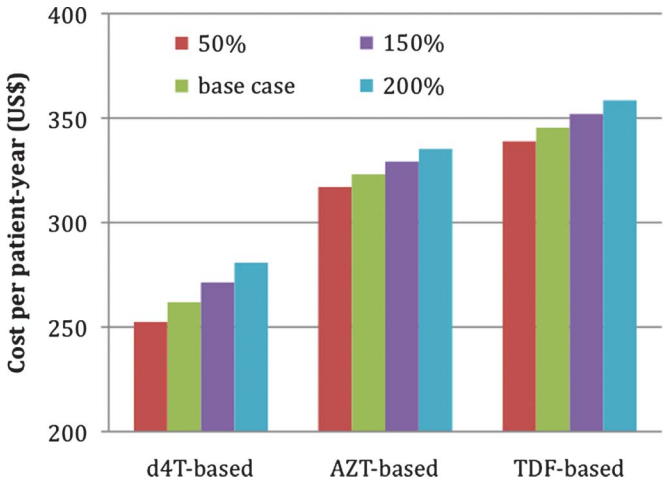

FIGURE 1. Impact of variations in the costs of treating HIV-related infections and toxicities on the overall cost per patient-year, by first-line regimen.

adverse events in the same cohort, the distribution of adverse events by drug was similar to those described in this study.[13] Potential for underreporting of adverse events due to the simplified approach to ART delivery in rural Lesotho is possible. However, the limitations of this setting reflect the reality of many high-HIV burden, resource-limited settings and the fact that this program was supported by clinicians experienced in HIV/TB care meant that this program received greater clinical oversight than many rural programs, giving us confidence that adverse event underreporting was unlikely. Possible limitations due to the duration of the study (median duration on ART being 508 days) also need to be considered. However, a recent 3-country study reported that the median time to toxicity was 141 days for d4T, 81 days for AZT, and 58 days for TDF.[17] The risk of longer-term adverse events are mostly associated with d4T, suggesting therefore that adverse events associated with d4T may have been underestimated in our study.[18]

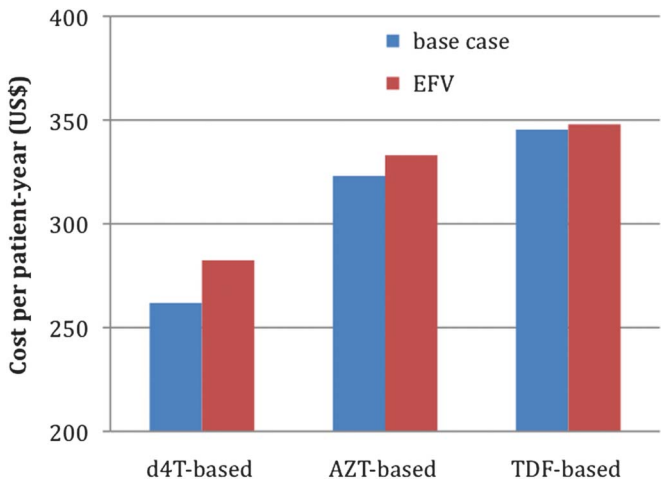

FIGURE 2. Impact of assuming that all patients receive EFV on the overall cost per patient-year, by first-line regimen

A further limitation of this study is that HRQoL was estimated by clinical staff using a visual analog scale, instead of alternative methods that might be preferred in health economics such as the standard gamble or the time trade-off (see details in **Supplemental Digital Content 4,** http://links.lww.com/QAI/A200).[9] Many of the resulting HRQoL values were lower than found in another study.[7] However, values in the latter study were either estimated using clinical experience or were taken from developed country studies and from different diseases (eg, peripheral neuropathy of the foot in diabetes patients). This suggests that additional research is needed to better understand the impact of side effects on HRQoL. We have adjusted for the uncertainty associated with these HRQoL measures by reporting outcomes as life years.

To facilitate implementation of TDF, political pressure should be exerted, supported by a clear demand from countries, to encourage further price reductions and additional generic manufacturing. Barely 10 years ago, it seemed unlikely that HIV would be treatable in sub-Saharan Africa due to the complexity of treatment and the cost of all ARV options. However, thanks to generic production, the cost of the most commonly used first-line regimen (d4T/3TC/NVP) has fallen from US $281 to US $61 per patient per year.[3] The price of TDF/3TC/EFV has fallen from US $426 to US $173 per patient per year in the last 4 years[19] while new synthesis processes and dose optimization studies suggest potential for further reductions in the price of TDF and partner drugs such as EFV. These efforts should be met by a firm commitment from donors and implementers to ensure that supply is met by a clear demand.

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