OPEN

The costs of HIV treatment and care in Ghana

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Objective: To determine cost functions that describe the dynamics of costs of HIV treatment and care in Ghana by $CD4^+$ cell count at treatment initiation and over time on antiretroviral therapy (ART).

Design: We used detailed longitudinal healthcare utilization data from clinical health records of HIV-infected patients at seven Ghanaian ART clinics to estimate cost functions of treatment and care by $CD4^+$ cell count at treatment initiation and time on ART.

Methods: We developed two linear regression models; one with individual random effects to determine the relationship between $CD4^+$ cell count at ART initiation and costs of treatment and care, and one with individual fixed effects to determine the causal effect of time in care on costs of treatment and care.

Results: Costs for treatment and care were lowest (−7.9 US$) for patients with $CD4^+$ cell counts of at least 350 cells/μl at ART initiation, compared with patients with 50 cells/μl or less at ART initiation, yet the difference was not significant. The per-patient costs peaked during the first 6 months on ART at 112.6 US$, and significantly decreased by 70% after 4 years on treatment.

Conclusion: Our findings show that an accurate analysis of resource needs of HIV treatment and care should take into account that healthcare costs for HIV-infected people are dynamic rather than constant. The cost functions derived from our study are valuable input for cost-effectiveness analyses and research allocation exercises for HIV treatment in sub-Saharan Africa.

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Introduction

Of the estimated 36.7 million individuals living with HIV worldwide in 2015, approximately 70% resided in sub-Saharan Africa (SSA) [1]. Nevertheless, in contrast to most countries in Eastern and Southern Africa, Western African countries are generally facing relatively low HIV prevalence levels. Ghana, one of the largest countries in West Africa in terms of population size, had an adult HIV prevalence of 1.6% in 2015 [2]. Antiretroviral therapy (ART) coverage in the country is suboptimal, with about 34% of all HIV-infected people receiving ART in 2015 [2]. The country is increasingly faced with difficult decisions on optimizing ART treatment strategies that are effective, efficient and feasible within the context of stagnating international donor contributions [3].

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Current treatment guidelines in Ghana specify ART eligibility at $CD4^+$ cell counts of 350 cell/μl or less [4]. In 2013, the WHO expanded the recommended ART eligibility to 500 cells/μl or less [5], and further to recommending treatment at any $CD4^+$ cell count in 2015 [6]. Increased treatment coverage and expanded eligibility are both important measures towards combating the HIV epidemic, yet they require an immediate increase in delegated funding [7].

In order for countries like Ghana to make decisions on ART delivery, comprehensive data on the costs of HIV treatment and care are essential [8]. These costs are dynamic, as the resource needs for monitoring and treating patients varies with disease stage. Disease stage varies both across individuals at treatment initiation [9–13] and may change within individuals through recovery as a result of effective treatment [14–16]. Accurately estimating per-patient costs of HIV treatment and care thus requires analysis of longitudinal observations of HIV-infected patients on ART to determine cost functions over time. However, most costing studies of HIV treatment and care in SSA are cross-sectional and only determined the costs of HIV treatment and care as a fixed per-patient cost, or cross-sectionally compared patients at different stages of care [15,17,18]. There are three studies that performed a longitudinal analysis: Leisegang *et al.* [16] described the costs of HIV treatment and care by using data from private-sector ART delivery in Southern Africa, Kimaro *et al.* [19] estimated the costs of HIV treatment and care in the 1st year of treatment for HIV-infected individuals at an advanced disease stage in Tanzanian public health centres and Harling and Wood [14] assessed the change in healthcare costs over time on ART for HIV-infected patients in a nongovernmental-organization-supported public sector ART programme in South Africa. As none of these studies corrected for unobserved confounding, the validity of the causal inference and generalizability to other settings is limited. A comprehensive costing study of HIV treatment and care, which can control for all unobserved time-constant confounding, and thus identify causal cost functions by time on treatment, is highly needed. The only available data on the cost of ART in Ghana to date is limited to interviews collected from health staff at healthcare facilities who were asked to estimate the costs of elements of HIV treatment and care [20].

We determined the costs of HIV treatment and care in Ghana by $CD4^+$ cell count at treatment initiation and time on ART by using detailed healthcare utilization data from clinical health records of HIV-infected patients at seven, mainly public-sector, Ghanaian ART clinics. The longitudinal nature of our data allowed us to accurately estimate cost functions of HIV treatment and care over time.

Methods

Setting

During September 2013, we collected data from clinical health records at seven ART clinics in Ghana at different levels of care. These clinics are vertically organized and purely concerned with HIV care, yet they are located on the premises of larger healthcare facilities. Two clinics were located at district hospitals, two at regional hospitals, one at a teaching hospital, one at a mission hospital and one at a private hospital. We specifically chose these clinics as these roughly represent the scope of care of ART delivery in Ghana. Five of the ART clinics were located in the Greater Accra region and two in the Eastern region.

Each clinic is required to have at least six healthcare workers trained on ART [21] including a doctor, a nurse, a counsellor and a pharmacist [22]. Ghanaian treatment guidelines state that patients should be followed up every 14 days in the first month after ART initiation, then monthly for the second and third month and every two to three months in the subsequent time in care [22].

Healthcare utilization data

At each clinic, research assistants were asked to randomly collect 50 clinical health records. The inclusion of clinical health records was based on two criteria: (1) the patient was aged 15 years or older at first registration in the clinic; and (2) the patient initiated ART during 2009, 2010 or 2011. The clinical health records exclusively hold information from visits at the respective ART clinics, and do not record information about additional care that HIV-infected patients may have received elsewhere.

We collected all healthcare utilization reported in the clinical health records at every appointment for all patients. Utilization included outpatient visits, inpatients stays, diagnostic tests and routine monitoring, antiretroviral drugs prescribed and non-antiretroviral drugs prescribed for opportunistic infections or other comorbidities. $CD4^+$ cell count at treatment initiation was defined as the last documented $CD4^+$ cell count prior to or on the date of ART initiation. Data were collected from first date of registration to December 2012.

Unit costs

We determined costs from a healthcare provider's perspective; patient-related costs such as lost wages, transportation costs and out-of-pocket expenses were not included. All unit costs were obtained from local sources, including a healthcare facility independent of this study but part of the Greater Accra Regional Health Directorate, henceforth referred to as the independent healthcare facility. The independent

healthcare facility was considered as a representable proxy of the different types of healthcare facilities included in the study.

Costs for outpatient visits consisted the salary for involved healthcare personnel during patient consultations. Salary structures were obtained from the Ghana Health Services (GHS), the governmental entity in charge of establishing pay structures for public hospitals in consultation with the Ministry of Health and the Ministry of Finance and Economic Planning. The salary structure for the private hospital was obtained directly from the healthcare facility. We retrieved costs for inpatient stays from the independent healthcare facility including costs for hospitalization, food, sanitation and documentation.

The unit costs for diagnostic tests and routine monitoring consisted of a combination of costs for the necessary testing equipment and salary for the time required for a laboratory technician to perform each test. The estimated costs of testing equipment were primarily collected from one of the providers of diagnostic services for governmental hospitals in Ghana, and when not available, were obtained from the independent healthcare facility.

Costs of antiretroviral drugs were obtained from the National AIDS Control Programme. We retrieved medication costs for all non-antiretroviral drugs recorded in the medical health records from the National Health Insurance Authority (NHIA) [23]. If unobtainable from the NHIA, medication costs were supplemented with data from the independent healthcare facility and a private pharmaceutical company. The costs of tuberculosis medication were obtained from the Global Drug Facility Product Catalogue [24].

All costs were corrected for inflation by using the health-specific consumer price index [25,26] with December 2012 as the reference period. All monetary values were converted to US dollars (US$) for the analysis by using the average exchange rate for the 31 December 2012 at a rate of 1 US$ to 1.899 Ghana Cedi [27].

We had to make several assumptions to translate observed healthcare utilization into costs, for example on-time allocation for healthcare personnel for specific tasks and of the pill count in prescriptions recorded in the clinical health records. All cost values and sources, as well as a detailed description of all assumptions made in the cost analysis are given in the Supplementary document, http://links.lww.com/QAD/B143.

Analysis

In this study, we defined the costs of HIV treatment and care as the total costs incurred for an individual patient in a 6-month period of care. For each patient visit at the ART clinics, we first multiplied all healthcare utilization reported in the clinical health records with the corresponding unit costs to determine the costs of HIV care and treatment data. Next, we stratified the data by $CD4^+$ cell count at ART initiation (eight categories: $\leq$50, 51–100, 101–150, 151–200, 201–250, 251–300, 301–350, $\geq$351 cells/μl) and by the time in care (in 6-month intervals). For patients with missing information on $CD4^+$ cell count at treatment initiation ($n = 40$), values were imputed using a multivariate normal model. This model uses a data augmentation algorithm to fill in missing data by drawing from a multivariate normal distribution, given the observed data [28]. For this study, the distribution was based on the first 6 months after ART initiation, as this was the period with most observations.

To determine the relationship between $CD4^+$ cell count at ART initiation and costs of treatment and care for HIV-infected patients in Ghana, we developed a multivariable linear regression model with individual random effects. The analysis controls for dependency of repeated observations within the same individuals. Costs of HIV treatment and care were analysed as the dependent variable and $CD4^+$ cell count at treatment initiation as the independent variable. The analysis only included costs that were incurred after ART initiation.

To determine the effect of time in care on costs of HIV treatment and care in Ghana, we developed a linear regression model with individual fixed effects to control for all unobserved time-constant confounding. By including individual fixed effects within regression models, we can correct for all characteristics of each individual that are constant over the observational period (e.g. sex, condition of the patient at the start of treatment, patient preferences for care, etc). Furthermore, this approach allows us to correct for selection effects, as the characteristics of patients observed only in the 1st year of treatment might not necessarily be comparable with those already on treatment for 3 to 4 years. The first 6 months after ART initiation were used as the reference period as this period contained observations on healthcare utilization in all patients. Costs of HIV treatment and care were analysed as the dependent variable and time since treatment initiation as the independent variable. All analyses were performed by using Stata version 1.2.1 (StataCorp, College Station, Texas, USA) and Microsoft Excel (Redmond, Washington, USA).

Sensitivity analysis

We performed univariate sensitivity analyses on all assumptions made in our main analysis. First, we assessed the impact of the imputations for missing $CD4^+$ cell count values at ART initiation by repeating the analysis, excluding cases missing $CD4^+$ cell count values. Second, we determined sensitivity of assumptions underlying the cost calculations in the main analysis of outpatient visits, inpatient stays, diagnostic tests and routine monitoring,

Table 1. Baseline characteristics of antiretroviral therapy clinics and patients from Ghana included in the study.

Data characteristics			
Number of ART clinics			
By type			
District			2
Regional			2
Mission			1
Teaching			1
Private			1
Total			7
By location			
Greater Accra region			5
Eastern region			2
Patient characteristics			
Number of patients			352[a]
Females			242 (69%)
Males			110 (31%)
Time in care (months)			
Mean time in care (IQR)			31.99 (30.77–33.23)
Mean follow-up time after ART initiation (IQR)			28.45 (27.38–29.52)
$CD4^+$ cell count at treatment initiation (by year of ART initiation)	2009	2010	2011
≤50 cells/μl	20	23	21
51–100 cells/μl	15	24	11
101–150 cells/μl	13	15	12
151–200 cells/μl	16	12	14
201–250 cells/μl	12	8	14
251–300 cells/μl	18	14	15
301–350 cells/μl	9	16	11
≥351 cells/μl	12	9	18
Total	115	121	116

ART, antiretroviral therapy.
[a]We aimed to collect 50 clinical health records at each ART clinics, yet 49 and 53 clinical health records were received from the private hospital and at one of the district hospitals respectively which led to a total of 352 clinical health records to be included in the full data analysis. IQR, interquartile range.

ART treatment, as well as medications prescribed for opportunistic infections or other comorbidities. All sensitivity analyses are described in the Supplementary document, http://links.lww.com/QAD/B143.

Ethics

Ethical approval was obtained from the Ethical Review Committee on research involving human patients managed by the GHS (ID-number: GHS-ERC 17/11/12).

Results

Table 1 shows the baseline characteristics of the ART clinics and the patients as recorded in the clinical health records. Among the total of 352 patients included in this study, 69% were women. The median follow-up time was 32 months in care and 28.5 months after initiating ART. One-third of the participants initiated ART with a $CD4^+$ cell count of 100 cells/μl or less, whereas approximately the same proportion had a relatively high $CD4^+$ cell count at ART initiation (≥250 cells/μl). No differences were found in the distribution of $CD4^+$ cell count categories over the years of treatment initiation (Table 1).

Figure 1 shows the average costs (US$) of care per patient over time for all patients (black line) and stratified by $CD4^+$ cell count at ART initiation (coloured lines). During the pre-ART period, the average costs of care per patient varied considerably both across time and between $CD4^+$ cell count categories, mostly due to relatively low numbers of observations. After ART initiation, however, the costs followed a more consistent pattern. Here, the average 6-monthly per-patient costs peaked at approximately 112.6 US$ during the first 6 months and sharply decreased in the subsequent 6 months to 74.1 US$, a reduction of 34.2%. During the remaining observational period, the costs per patient declined more steadily before ending at 33.9 US$, 4 years after ART initiation (a 70% decrease in costs compared with the first 6 months) (Fig. 1).

Figure 2 shows a breakdown of cost components of treatment and care for HIV-infected people in Ghana by time in care. Although the costs for ART drugs comprised 46.1% (51.9 US$) of the overall costs during the first 6 months on ART, these costs constituted a much larger part of the total costs of HIV treatment and care after 4 years on ART (71.7%). Furthermore, the proportion of the total costs accounting for outpatient visits declined from 11.3 to 9.6%, for inpatient stays from 3.6 to 0%, for diagnostic tests and routine monitoring from 3.6 to 1.3% and for non-antiretroviral drugs prescribed for opportunistic infections or other comorbidities from 35.4 to 17.5% over the same 4-year period.

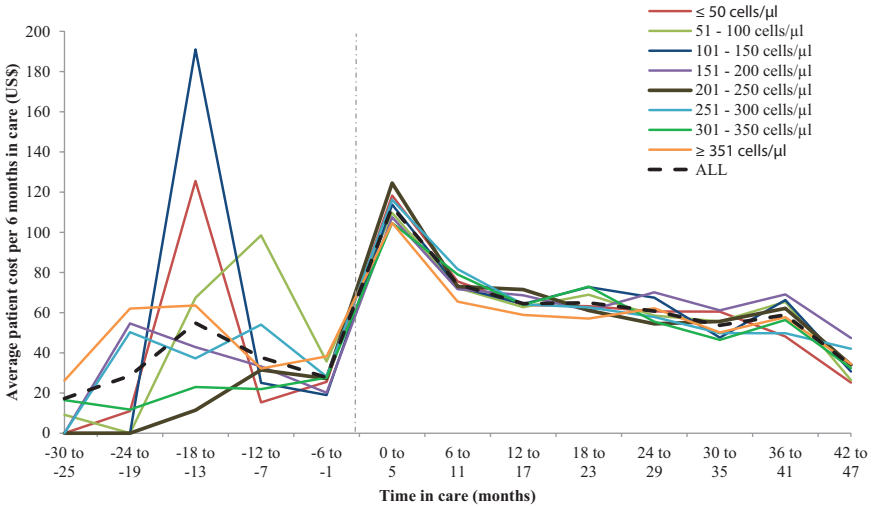

Fig. 1. Per-patient costs of HIV treatment and care over time in care. The figure shows data from all seven healthcare facilities. It shows the average costs (US$) of treatment and care per patient at the antiretroviral therapy clinic over time and stratified by $CD4^+$ cell count at treatment initiation (coloured lines), as well as aggregated across all $CD4^+$ cell count categories (black line). Costs are presented in 6-monthly periods since treatment initiation, negative time represents preantiretroviral therapy care and the grey dashed line shows the moment of treatment initiation.

Table 2 shows the results of the multivariate linear regression with individual random effects of 6-monthly per-patient costs on $CD4^+$ cell count at treatment initiation, corrected for sex, time on care and healthcare facility. The lowest costs were found for patients with a $CD4^+$ cell count of 351 cells/µl or higher, which was −7.9 US$ lower compared with patients with a $CD4^+$ cell count of 50 cells/µl or less. Nevertheless, the differences in costs of HIV treatment and care after ART initiation between the $CD4^+$ cell count categories were not significant (Table 2).

Table 3 shows the results of the linear regression of 6-monthly per-patient costs on time since treatment initiation, with individual fixed effects to correct for all time-constant confounding. Per-patient costs significantly declined over time. Compared with the first 6 months of ART, costs declined with 38.6 US$ in the second 6 months period on ART. After 4 years on ART, costs were 84.6 US$ lower compared with the costs at initiation.

Our findings were mostly not sensitive to changes in assumptions of key parameters. In 20 out of 28 sensitivity

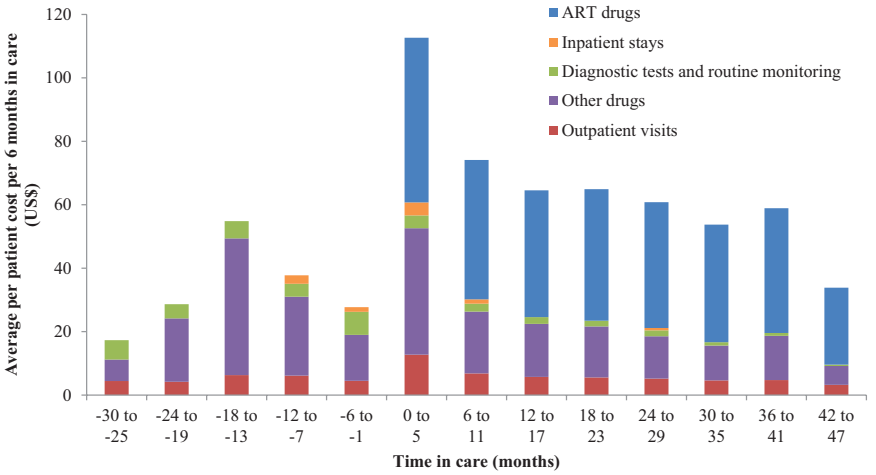

Fig. 2. Breakdown of cost components of treatment and care for HIV-infected people in Ghana, by time in care. Costs are presented in 6-monthly periods since treatment initiation, negative time represents preantiretroviral therapy care. Costs are broken down into costs for antiretroviral therapy drugs, inpatient stays, diagnostic tests and routine monitoring, other drugs and outpatient visits, and are aggregated over all $CD4^+$ cell count categories.

Table 2. Multivariable linear regression of per-patient costs of HIV treatment and care on $CD4^+$ cell count at antiretroviral therapy initiation in Ghana.

	Total costs (US$) (95% CI)	*P* value
Intercept	106.6 (98.2–115.0)	<0.0001
$CD4^+$ cell count at ART initiation (cells/μl)		
≤50	0	–
51–100	2.7 (−4.9; 10.3)	0.490
101–150	−0.2 (−8.4; 7.9)	0.953
151–200	0.9 (−7.1; 8.8)	0.833
201–250	−1.5 (−10.1; 7.0)	0.723
251–300	−0.7 (−8.5; 7.1)	0.867
301–350	−1.4 (−9.8; 7.0)	0.747
≥351	−7.9 (−16.1; 0.3)	0.058
Time after ART initiation (months)		
0–5	0	–
6–11	−38.5 (−43.5; −33.6)	<0.0001
12–17	−48.0 (−53.1; −43.0)	<0.0001
18–23	−48.8 (−54.1; −43.6)	<0.0001
24–29	−53.8 (−59.6; −48.1)	<0.0001
30–35	−61.6 (−68.0; −55.2)	<0.0001
36–41	−57.3 (−64.9; −49.8)	<0.0001
42–47	−81.5 (−93.3; −69.8)	<0.0001
Sex		
Male	0	–
Female	−2.8 (−7.5; 1.8)	0.225
Healthcare facility		
HF 1	0	–
HF 2	−3.3 (−11.2; 4.7)	0.418
HF 3	8.8 (0.8; 16.9)	0.031
HF 4	20.0 (12.2; 27.7)	<0.0001
HF 5	15.4 (7.4; 23.5)	<0.0001
HF 6	4.9 (−3.0; 12.8)	0.226
HF 7	15.2 (7.3; 23.2)	<0.0001

Model with trends in per-patient costs of 6 months of HIV treatment and care over $CD4^+$ cell count at treatment initiation, corrected for time on ART, sex and treatment facility are shown. The regression model contains individual random effects to control for dependency of observations in the same individual. ART, antiretroviral therapy; CI, confidence interval.

analyses, all point-estimates were within the confidence interval of the main analyses. In addition, none of the alternative assumptions in the sensitivity analysis changed the shape of the cost functions over $CD4^+$ cell count of treatment initiation or time since ART initiation. All results and more details of the sensitivity analyses can be found in the Supplementary document, http://links.lww.com/QAD/B143.

Discussion

We performed a comprehensive analysis of the costs of treatment and care for HIV-infected patients at ART clinics in Ghana, and we described cost functions by $CD4^+$ cell count at initiation and time in care. Our data show a significant change in overall costs per patient as an effect of time in care, irrespective of $CD4^+$ cell count at treatment initiation. The per-patient costs peaked during the first 6 months after ART initiation at 112.6 US$, and subsequently decreased by about 70% after 4 years on treatment. The decrease was largely driven by a decline in medications for opportunistic infections or other comorbidities.

Table 3. Change in per patient costs of HIV treatment and care as an effect of time in care in Ghana.

Time in care (months)	Total costs (US$) (95% CI)	*P* value
−25 to −30	−90.8 (−134.4; −47.2)	<0.0001
−19 to −24	−90.0 (−114.4; −65.6)	<0.0001
−13 to −18	−68.5 (−82.5; −54.5)	<0.0001
−7 to −12	−80.6 (−91.1; −70.2)	<0.0001
−1 to −6	−85.3 (−90.8; −79.9)	<0.0001
0–5	0	–
6–11	−38.6 (−43.9; −33.2)	<0.0001
12–17	−48.0 (−53.4; −42.5)	<0.0001
18–23	−50.1 (−55.8; −44.5)	<0.0001
24–29	−56.4 (−62.6; −50.1)	<0.0001
30–35	−64.9 (−71.8; −57.9)	<0.0001
36–41	−60.6 (−68.9; −52.3)	<0.0001
42–47	−84.6 (−97.5; −71.7)	<0.0001

Multivariable linear regression of per-patient costs of HIV treatment and care on time since ART initiation in Ghana. Model with trends in per-patient costs of 6 months of HIV treatment and care, with the first 6 months after ART initiation as the reference period. The regression model contains individual fixed effects to control for unobserved time-constant confounding. ART, antiretroviral therapy; CI, confidence interval.

To our knowledge, this is the first study for any West African setting to determine cost functions for HIV treatment and care over time by using longitudinal data, and the first study from SSA to provide causal cost functions for HIV treatment and care by time on treatment. The results from our study are in line with findings from other studies in SSA, showing that costs for HIV treatment and care decrease over the course of ART, largely due to a decline in opportunistic infections, diagnostic test and routine monitoring and hospitalization. However, these studies either only collected cross-sectional data [15,17,18], analysed longitudinal data within a limited timeframe of 1–2 years on treatment [14,19] or only analysed data from private-sector clinics [16]. Furthermore, none of these studies corrected their results for unobserved confounding. We performed a comprehensive, longitudinal data collection of healthcare utilization over periods of up to 4 years in care, and performed individual fixed-effects regression analysis to develop causal and generalizable cost functions by time on treatment, which will not only be useful for the Ghana setting, but also can be applied to budgeting and cost-effectiveness studies throughout SSA.

The findings in this study are of great value for assessing resource allocation for HIV in Ghana and other SSA countries in general. Evidence for resource allocation in HIV treatment is commonly generated by using mathematical modelling, yet so far, most modelling studies provide projections over time by using one constant cost value for HIV care after ART initiation [29–31], ignoring the dynamics of changing costs over time. We show that healthcare costs for HIV-infected people are dynamic

rather than constant, and that an accurate analysis of future resource needs or cost-effectiveness of treatment interventions should take this into account. Our results show that costs of treating patients over time decreases after ART initiation as the health of HIV-infected patients increase, resulting in decreased need for healthcare utilization. As ART programmes mature, the patient mix changes and more and more patients will be relatively symptom-free, thus requiring less healthcare resources. Consequently, the overall costs per-patient will decline.

We did not find a significant relationship between $CD4^+$ cell count at treatment initiation and costs for HIV treatment and care, even though our data showed slightly decreasing costs with increasing $CD4^+$ cell counts at initiation. A possible explanation for this is that case detection in Ghana is still very much driven by symptom-based health seeking rather than active case finding and regular testing of asymptomatic HIV-infected people, resulting in selection bias towards more severely ill patients in our data, regardless of $CD4^+$ cell count. Another potential reason could be that the clinical health records from the ART clinics only contain information on healthcare utilization at the ART clinic. If we would have been able to also capture healthcare utilized at other facilities, we might have had more power to detect differences in costs by $CD4^+$ cell count at treatment initiation.

There were some limitations to our study. First, patients in our study were observed for a maximum of 4 years after treatment initiation, and it is unknown how the cost of HIV treatment and care would develop for patients on treatment beyond the time-frame of our study. However, as treatment costs already started to level off at the end of the observational period, we believe that further changes after our observational period are likely to be limited. Second, as most of the patients in this study had a $CD4^+$ cell count below 350 cells/μl, it was not possible to capture costs for patients with higher $CD4^+$ cell counts at treatment initiation, as recommended by the WHO [6]. Third, the clinical health records were article-based, sometimes leading to difficulties in interpreting the data as well as concerns of missing information. However, missing information is likely to be random, and therefore not likely to influence the estimated cost functions. In addition, local field personnel were included in the data collection to report as accurate information as possible about the healthcare utilization. Fourth, several assumptions had to be made to translate observed healthcare utilization and medication uptake into meaningful units for cost calculations, for instance with regards to duration of drug prescriptions and staff consultation at outpatient visits. Although the duration of each prescription of antiretroviral drugs was based on recommended follow-up frequency of outpatient visits in the national guidelines of ART [22], we found that practice does not always follow guidelines, as many patients did not visit the health facility according to the frequency stated in the guidelines. In addition, whereas the costs of outpatient visits are based on salary of attending staff, the costs for healthcare personnel may also include time on other tasks than direct patient consultation. However, it is reassuring that changes to these assumptions in the sensitivity analysis did not affect the main outcomes of the study.

In conclusion, this study showed that the costs of HIV treatment and care in Ghana reduce substantially during the course of ART for HIV-infected people. This is the first detailed cost analysis of HIV treatment and care in Western Africa and provides important data for policy makers and researchers when determining resource needs and cost-effectiveness for HIV treatment and care programmes.

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Conflicts of interest

There are no conflicts of interest.

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