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Potential health gains in West and Central Africa through savings from lower cost HIV treatment

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\textbf{Objective:} Prices of antiretroviral (ARV) drugs in lower income countries have decreased substantially over the past two decades, helping to facilitate greatly expanded access to antiretroviral therapy (ART). However, ART coverage in many parts of the world remains low. We investigate the extent of epidemiological benefits that might be expected if ARV drug prices decline further.

\textbf{Design:} A modeling study using data from seven countries in West and Central Africa (Cameroon, Democratic Republic of the Congo, Côte d’Ivoire, Niger, Nigeria, Senegal, and Togo).

\textbf{Methods:} We investigated how the timing of ARV cost reductions could affect the impact and compared three different possible investment strategies: reinvesting in ART, reinvesting in the HIV response according to historical allocations, and reinvesting with the aim of minimizing HIV incidence and mortality.

\textbf{Results:} If ARV drug prices fell by 37\% relative to 2018 levels (i.e. following continued trend declines), we calculate ART unit costs could decrease by \textasciitilde20\% (holding other cost components constant). If this could be achieved by 2020 and the savings were reinvested into ART, we estimate that an additional 8\% of HIV infections and 11\% of HIV-related deaths could be averted over 2020–2030 across the seven countries. Slightly greater gains could be attained if funds were reinvested in ART in combination with primary prevention. Delays in the year of introduction of ARV price reductions would reduce the impact by about 1\% per year.

\textbf{Conclusion:} ARV price reductions could free up funds that – if strategically invested – would help countries move closer toward the elimination of HIV.

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\textbf{Introduction}

Effective antiretroviral therapy (ART) reduces morbidity, mortality and onward transmission of HIV [1–3]. Consequently, there has been global focus on increasing the percentage of people living with HIV (PLHIV) receiving effective virally suppressive ART, with countries having committed to achieving 73\% viral suppression among PLHIV by 2020, in line with the UNAIDS 90–90–90 targets [4]. Notwithstanding the political commitment to this target, there is significant disparity in progress across regions, countries, and populations. In particular, those from key or marginalized populations who are often at the highest risk of acquiring and transmitting HIV are often those left behind [5].

In testament to the global commitment to providing ART for all PLHIV, there has been significant focus on negotiating drug pricing agreements that would enable all
countries [but especially low-income and middle-income countries (LMICs)] to provide treatment at affordable prices. The recommended price of first-line antiretroviral (ARV) regimens had already decreased from ~US$10,000 per patient per year to US$143 per patient per year over 2000–2014 in countries eligible to use generics [6], thanks in large part to exemptions introduced to international patent laws. Despite past studies pessimistically predicting limited scope for further reduction in the price of ARVs, by 2018 it had decreased by another 50% to around US$72 per patient per year [7].

One cause for optimism with respect to future ARV pricing is the development, approval, and adoption of new generic drug regimens. In September 2017, UNAIDS announced a pricing agreement accelerating the availability of the first affordable, generic, single-pill HIV treatment regimen containing dolutegravir (DTG) to public sector purchasers in low-income and middle-income countries [8]. Since then, the TLD regimen [consisting of tenofovir disoproxil fumarate (TDF), lamivudine (3TC) and DTG] has become the WHO-preferred first-line regimen for nearly all adults and adolescents, and two dozen high-burden LMICs have already included or are planning to include this in their national HIV treatment guidelines [7]. At a cost of around US$72 per person per year in 2018, DTG-based regimens are helping drive down the costs of ART provision, both because of the increasing market share they are expected to occupy (~62% of the adult first-line market in LMICs by 2022) and because of the downward pressure that such alternatives exert on other regimens [7]. Further on the horizon, the introduction of long-acting ARVs (administered via injection/implantation; currently in phase 3 trials) have the potential to reduce drug costs even further (although scope for reduction may depend on price floors for the active ingredients [9]). Although drug prices are just one of the components of ART provision, there is nevertheless considerable evidence that at least some of these rapid declines in recommended ARV prices are lowering the cost of providing high-quality ART [10]. By reinvesting savings from cheaper drug prices into the HIV response, countries may be in a position to reach targets that were previously well out of reach.

In 2016, only 25% of PLHIV in West and Central Africa (WCA) were virally suppressed, making it one of the regions lagging furthest behind the 73% target [5]. Low coverage of ART has corresponded to a disproportionately high number of HIV-related deaths in the region: although just 7% of the world’s population live in the region, it accounts for 30% of the world’s HIV-related deaths. One possible explanation for this could be that the HIV epidemic in WCA is far more concentrated among key populations than epidemics in Southern and Eastern Africa [11], and there are strong indications that key populations in WCA face substantial barriers to accessing essential health services, including extremely low access to ART. In 2013, estimated HIV prevalence was 34.9% among female sex workers (FSWs), 7.3% among their clients, 17.7% among MSM, and 3.8% among people who inject drugs (PWID) in WCA [11].

In this study, we estimate the health gains that may be possible if ARVs could be procured at lower cost across WCA, and illustrate how these gains change with delays in attaining cost reductions. To generate these projections, we gathered epidemiological, demographic, and programmatic data from seven countries in WCA constituting 78% of the total number of PLHIV in the region (Cameroon, Democratic Republic of the Congo, Côte d’Ivoire, Niger, Nigeria, Senegal, and Togo). Although the magnitude of savings to the treatment budget that new treatment regimens could be expected to deliver is not entirely clear, it is nevertheless relevant to pose the general question of what epidemiological impact a hypothetical reduction in ART unit costs might have.

Methods
Modelling framework
These analyses used Optima HIV [12], a compartmental model of HIV transmission and disease progression linked to a programmatic response module, which is capable of estimating the optimal allocation for the HIV budget across a mixture of programs to produce the outcome best aligned with particular targets. Optima HIV is described in detail elsewhere [13,14].

Epidemic input data and model calibration
For each country, the epidemic model component of Optima HIV was populated with country-specific behavioral, clinical, demographic, and programmatic data, with key country-specific model inputs and sources summarized in Table S1, http://links.lww.com/QAD/B558. Additional noncontext-specific parameters are summarized in the Optima HIV User Guide [15]. For each country, the model was initiated in the year 2000 and calibrated to available data and estimates on HIV prevalence, population sizes, number of people on treatment, number of PLHIV, and the state of the care cascade. Uncertainty estimates were generated around the model projections using an Approximate Bayesian Computation (ABC) algorithm, with prior distributions defined over model parameters. By sampling from the prior distributions, we obtained a set of possible epidemic outcomes in each year from 2000 to 2017 inclusive. Calibration outputs are shown in Figures S1 and S2, http://links.lww.com/QAD/B558.

HIV program data
We gathered data from National AIDS Spending Assessments (NASAs) and other sources on the allocation
of HIV resources across broad programmatic categories (Fig. 1). As in Kelly et al. [16], we distinguish between targeted and nontargeted HIV programs, with the former constituting treatment and prevention programs that have a direct proximal effect on reducing HIV transmission, morbidity, or mortality. Programmatic spending across targeted programs was linked to behavioral outcomes using country-specific cost functions published in the appendix to Kelly et al. [16].

**Approximating potential future antiretroviral therapy unit cost reductions**

Firstly, we needed an estimate of ART unit costs for each country, as well as the share of these costs attributable to ARVs. For each country, we found the latest year for which country-reported estimates of overall expenditure on ART were available, and divided by the number of people who were receiving ART in that year to give an estimate of the spend per person on ART. We use these top–down estimates to approximate the unit cost of delivering ART in each country; although crude, these estimates are comparable with those available via the Global Health Costing Consortium’s unit cost study repository (Table S2, http://links.lww.com/QAD/B558) [17].

Next, we obtained 2018 antiretroviral spending data from the UNAIDS HIV Financial Dashboard and used these to calculate the average weighted cost of providing ARVs in each country (Table S2, http://links.lww.com/QAD/B558). As these estimates are for 2018, we back-projected them to obtain an estimate of the average weighted cost of providing ARVs in the year for which our top–down ART unit cost estimates applied using an assumed average annual price fall of 14% (as per reported global trends over the past 10 years [7]). We could then disaggregate our top–down ART unit costs into ARV-related and non-ARV related components (Table S2, http://links.lww.com/QAD/B558).

To create projections of future ART unit costs, we assumed the non-ARV-related components for ART delivery remained constant. We acknowledge this is most likely not a realistic assumption, as there is a wealth of evidence to indicate that the future trajectory of these component costs are likely to vary significantly [10]. However, as our focus is to highlight how ARV price reductions may impact on ART costs, we take a ‘ceteris paribus’ approach and hold all other factors constant.
Finally, we investigated the potential impact of further ARV price reductions. We remain agnostic about the timing or causes of this decrease: it could be that prices will continue to decrease steadily year-on-year, as they have for the past 10 years, or it could be that prices remain stable for some years before new pipeline regimens come on the market and further drive down costs (in the following section on model analysis, we discuss how we analyzed the effects of timing for a further assumed reduction in ARV prices). We investigated three possible trajectories for future ARV prices: a median trajectory assuming there is potential for a further 37% reduction in ARV prices by 2030 (i.e. assuming that the trend average annual price reduction of ~14% over the past 10 years continues for 3 more years); a conservative trajectory assuming a further 10% reduction in ARV prices by 2030; and an optimistic trajectory assuming a further 50% reduction in ARV prices by 2030, all compared with 2018 levels. Combining these price fall assumptions with the assumption that the non-ARV-related components of the ART program remain constant, we derived an average hypothesized reduction in ART unit costs of 20% in the median scenario, 10% in the conservative scenario, and 25% in the optimistic scenario. Full details are in Table S2, http://links.lww.com/QAD/B558.

Model analysis
Firstly, we considered how the timing of an ARV price reduction affects the epidemiological impact that could be expected under the median, conservative, and optimistic trajectories. We construct a set of scenarios by varying the year of introduction of the lower prices from 2020 to 2030. We then assume that all savings from this price reduction are reinvested in the ART program, and calculated the number of PLHIV, new HIV infections, and HIV-related deaths averted over 2020–2030 inclusive relative to the baseline scenario in which ARV prices are assumed to remain at 2018 levels.

Secondly, we assumed that the ARV price reduction is introduced in 2020 and leads to a 20% reduction in ART unit costs (i.e. the median trajectory described in the previous section), and we considered three different investment strategies for the additional funding that would be freed up by this reduction:

1. Savings reinvested in the ART program;
2. Savings reinvested in the HIV response and distributed according to historical patterns (shown in Fig. 1);
3. Savings reinvested in the HIV response in such a way as to minimize the sum of cumulative HIV infections and cumulative HIV-related deaths over the 2020 through 2030 period, inclusive of the start and end years. For brevity, we refer to this as the ‘health maximizing’ investment plan, although we note that many alternative definitions of health maximization exist.

For each scenario, we report the model-generated estimates of the number of PLHIV, new HIV infections, and HIV-related deaths over 2020–2030 inclusive. We compare these to a ‘status-quo’ scenario assuming no change in ARV costs or to the total HIV budget.

Results
Impact of timing cost reductions
In Fig. 2, we summarize the incidence and death reductions that could be attainable across the seven countries in the region, depending on the year in which the ARV cost reductions are assumed to begin. The sooner that ARV unit costs can be reduced, the greater the estimated epidemiological impact. This is the case no matter which price reduction scenario we consider, although the impact would certainly be greater if larger ARV price falls could be attained.

Analyzing reinvestment strategies
A summary of the epidemiological outcomes associated with the four different investment strategies (i.e. status-quo with the three scenarios in which ART unit costs are assumed to decrease) is presented in Fig. 3 and in Table S3, http://links.lww.com/QAD/B558. HIV budget allocations under each scenario are presented in Figure S3, http://links.lww.com/QAD/B558 and Table S4, http://links.lww.com/QAD/B558. Compared with the status quo scenario where ART unit costs remain at historical levels, all three scenarios where ART unit cost reductions were considered would deliver epidemiological benefits. Scenario 2, in which we assume the savings from a 20% reduction in ARV costs are reinvested in the ART program, could lead to further reductions in cumulative infections of up to 9% and in cumulative deaths of 13% by the end of 2030 across the region (Fig. 3).

For all seven countries, we also estimated the health-maximizing allocation of the savings gained from the assumed 20% reduction in ART unit costs (Scenario 4), and found that further improvements could be possible in most cases. In Cameroon, it would afford the opportunity for a 28% scale-up in the country’s PMTCT program, which would bring coverage of this program from an estimated 77% in 2018 [25] to 95% by 2020, as required for eliminating mother-to-child transmission (MTCT) [26]. The subsequent reduction in MTCT cases would lead to a reduction in cumulative new infections of 16% relative to status quo, 6% relative to reinvesting the savings in ART, and 5% relative to reinvesting the savings according to historical patterns (over 2020–2030 inclusive).

In Côte d’Ivoire, the health-maximizing allocation would allow for a tripling of coverage of FSW programs. Not
only would this reduce incidence in the FSW population itself, but is also estimated to be the best means of reducing onward transmission to clients of FSW and older men, both of which contribute substantially to the overall incidence in the country [27]. Increasing coverage of FSW programs would also help address the weaknesses in the diagnosis and linkage to care for FSW; according to PEPFAR estimates, only 65% of FSW identified as HIV-positive are linked to ART [28]. Reinvesting savings from ARV price reductions into FSW programs could lead to an estimated 19% reduction in cumulative new infections over 2020–2030 inclusive relative to status quo, and a 11% reduction relative to reinvesting the savings in the ART program or according to historical investment patterns.

In DR Congo, we find that the highest priority areas under the health-maximizing allocation are programs targeting FSW and MSM, HIV testing, and linkage programs targeted at the general population, and providing additional ART. Historically, investment in FSW programs has been low, with just over US$ 6000
invested in 2014 to cover 56,000 sex workers, leaving significant scope for scale-up. With an estimated 59% of PLHIV aware of their status and 55% of PLHIV receiving treatment in 2018, investment in both testing and treatment programs is a priority. Relative to the baseline scenario, we estimate that reinvesting savings from an ARV unit cost reduction across these priority areas could deliver a 20% reduction in cumulative incidence over 2020–2030 inclusive, and a 4% reduction in cumulative deaths. Relative to reinvesting these savings in the ART program or according to historical patterns, this strategy could avert an additional 19 or 17% of cumulative infections, respectively, and 3% of cumulative deaths.

In Niger, FSW programs were also identified to be a priority for scale-up, again in the context of the low levels of investment in these programs historically. Reinvesting savings from ARV cost reductions into FSW programs is estimated to lead to an 8% reduction in cumulative new infections over 2020–2030 relative to status quo and a 5% reduction in cumulative deaths, or a 5–6% reduction in infections and a 1–2% reduction in cumulative deaths relative to reinvesting the savings in the ART program or according to historical investment patterns, respectively.

In Nigeria, we find that the health-maximizing strategy would be to reinvest savings from an ARV cost reduction towards ART (i.e. equivalent to scenario 2). Nigeria has a very large treatment gap with just 33% of PLHIV having received treatment in 2018. If ARVs could be procured at cheaper prices, Nigeria would be able to partially address this treatment gap, with a scale up to 39% by 2020 even without investing additional funds. Relative to baseline, this could avert an additional 9% of cumulative infections and 13% of cumulative deaths over 2020–2030 inclusive, and relative to reinvesting according to historical patterns, the percentages of additional infections and deaths that could be averted are 3 and 5%, respectively.

In Senegal, scale-up of FSW programs (by 30%), HIV testing programs targeted at the general population (by 200%), and PMTCT (by 16%) are prioritized. This reinvestment strategy could lead to an estimated additional 17% reduction in cumulative new infections over 2020–2030 inclusive relative to status quo, and an additional 10% reduction in cumulative deaths. The number of cumulative infections estimated to result from this investment strategy is similar (or even very marginally higher) to reinvesting in the ART program or according to historical investment patterns, but cumulative deaths are estimated to be 3% lower.

In Togo, we estimate that the scope for epidemiological improvements from reinvesting ARV price reductions could be greater than for any other country in the region. Reinvesting the additional funds to minimize incidence and mortality could lead to an estimated additional 40% of cumulative infections being averted and 52% of cumulative deaths over 2020–2030 compared with status quo, 21 and 16% compared with reinvesting in ART, and 14 and 15% compared with reinvesting according to historical patterns. This would be achieved by prioritizing PMTCT and improving coverage of pregnant women receiving ARVs (at 66% in 2018), as well as HIV-testing programs targeted at the general population.

Discussion

We examined the impact of reductions in ART unit costs in seven countries in WCA. Unsurprisingly, we found that the sooner ARV prices decrease, the better the epidemiological impact attainable from reinvesting the savings. By country, we found that reinvesting savings to minimize cumulative new infections and HIV-related deaths could lead to additional reductions of 8–40% in cumulative new infections and 4–52% in cumulative HIV-related deaths over 2020–2030. Aggregating results for all seven countries, we estimate that an additional 11% of cumulative new infections and 13% of cumulative deaths could be averted.

We found that the health-maximizing reinvestment strategy was country-specific, supporting the idea that the best outcomes come from tailoring the response to the epidemic rather than applying general rules to guide investment allocations [16,29]. In countries where HIV awareness was particularly low, HIV testing and linkage to care were prioritized. In Côte d’Ivoire, DR Congo, Niger, and Senegal, FSW programs were prioritized because of the significant transmission effects associated with sex work in these countries [23,27,30]. On the other hand, whilst programs for FSW in Nigeria and Togo are important to maintain, greater epidemiological benefit is estimated to be possible by targeting HIV testing and linkage to care, treatment scale-up, and PMTCT. In any given context, there may be a great deal to consider when thinking about how to best orient the HIV response. Mathematical modeling plays an important role in helping to process these data and translate them into clear policy recommendations to support decision-making.

Although additional epidemiological gains may be possible through allocating resources to minimize incidence and mortality, our model analyses indicate that these gains are overshadowed by the gains that would result from simply having more funds available to invest in the HIV response. An immediate implication of this is that improvements in strategic purchasing of health services would likely pay large dividends. Although empirical studies on health service purchasing are limited, a study of the health system in Nigeria found little evidence of strategic purchasing [31], and issues have also been identified across LMICs more broadly [32].
In this study, we estimated the impact of hypothesized reductions in ART unit costs, and did not identify the exact mechanisms through which such reductions might be attained. One possibility is the introduction of HIV treatment regimens containing dolutegravir (DTG) to public sector purchasers in LMICs [8]. A study by Phillips et al. [33] found that the benefits of transition to tenofovir, lamivudine, and dolutegravir for all substantially outweighed the risks. However, given the continued uncertainties regarding the introduction of DTG-based regimens into national protocols, we did not want to present analyses that relied too heavily on this being a near-term policy. We also did not consider other sources of uncertainty around future drug pricing agreements, some of which could indeed cause ART unit costs to increase [6]. Another limitation stems from the difficulties in getting timely and complete data on intervention costs and HIV budget allocations. The best sources for these data are often country NASA reports but these are often out-of-date and have significant data gaps. We had to rely on expenditure data from 2013 for two countries and 2014 for three countries, and although we adjusted investments to account for the known scale-ups in ART in the intervening years, we did not have sufficient data to scale other programs. Therefore, the baseline budget allocations used in this work should be considered as indicative of general trends rather than as an accurate picture of recent finances.

Progression towards viral suppression targets in WCA must focus on engaging populations with the greatest burden of disease across the continuum of HIV care. Savings on drug procurement have the potential to free up funds, and by strategically reinvesting these savings, countries may have new opportunities for improving health outcomes and moving closer towards eliminating HIV.

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Conflicts of interest

There are no conflicts of interest.

References


