Characterising the scale-up and performance of antiretroviral therapy programmes in sub-Saharan Africa: an observational study using growth curves

Benjamin Bigelow, Stéphane Verguet

ABSTRACT

Objectives The rate of change in key health indicators (e.g., ART coverage) is an understudied area of health system performance. Rates of change in health services indicators can augment traditional measures that solely involve the absolute level of performance in those indicators. Growth curves are a class of mathematical models that can parameterise dynamic phenomena and estimate rates of change summarising these phenomena; however, they are not commonly used in global health. We sought to characterise the changes over time in antiretroviral therapy (ART) coverage in sub-Saharan Africa using growth curve models.

Design This was a retrospective observational study. We used publicly available data on ART coverage levels from 2000 to 2017 in 42 sub-Saharan African countries. We developed two ordinary differential equations models, the Gompertz and logistic growth models, that allowed for the estimation of summary parameters related to scale-up and rates of change in ART coverage. We fitted non-linear regressions for the two models, assessed goodness of fit using the Bayesian information criterion (BIC), and ranked countries based on their estimated performance drawn from the fitted model parameters.

Results We extracted country performance in rates of scale-up of ART coverage, which ranged from ≤2.5 percentage points per year (South Sudan, Sudan, and Madagascar) to ≥8.0 percentage points per year (Benin, Zimbabwe, and Namibia), using the Gompertz model. Based on BIC, the Gompertz model provided a better fit than the logistic growth model for most countries studied.

Conclusions Growth curve models can provide benchmarks to assess country performance in ART coverage evolution. They could be a useful approach that yields summary metrics for synthesising country performance in scaling up key health services.

INTRODUCTION

Health policy-makers are concerned with measuring the effectiveness, efficiency and overall performance of national health systems in a comparable manner. Measuring performance requires relating the attainment of specific objectives, such as the improvement of population health and of its distribution, to the dedicated financial resources and expenditures in a country. Additionally, comparable data on health system performance provide a foundation for subsequent analyses of variation across countries, ultimately strengthening the evidence base for understanding variations in performance and for policy implementation. Stakeholders can then use such information to better analyse how performance on stated objectives varies with several factors, including how the health system is organised, financed and regulated.

The question of how to evaluate health system performance is difficult, as it requires choices to be made about what to measure (e.g., outcomes, outputs and costs), how to measure (e.g., with which administrative data, household surveys), and how to present the results (e.g., with which individual or composite indicators). For example, in its 2000 World Health Report, the WHO defined health system performance along several objectives and then ranked the health systems of WHO member states using statistical modelling. This generated immediate debate and a number of researchers subsequently revisited the methodology and the sensitivity behind the rankings.
A step towards understanding country performance in health could lie in the examination of the evolution over time of specific health outcomes and health services indicators. However, many health indicators focus on the absolute level of performance. The United Nations’ Millennium Development Goals, for example, included health outcomes such as the maternal mortality ratio and the incidence of malaria, two indicators that capture performance at a single point in time.\(^\text{11}\) Similarly, UNAIDS developed performance indicator levels into its recent 90-90-90 treatment targets for tackling the AIDS epidemic by 2030.\(^\text{12}\) Yet, only evaluating the levels of performance for certain outcomes can ignore longstanding determinants within countries that may affect the ability to expand access to care. It may also blur the ability of researchers to understand performance variation across countries. In this respect, examining the rates of change in health services indicators may prove valuable in understanding the performance of national policies and programmes.\(^\text{15-17}\) As a case in point, in Good Health at Low Cost: 25 Years On, Balabanova et al.\(^\text{16}\) used both levels and rates of changes of health outcomes and services coverage to select which countries to study as relevant examples of good performance in health.

Rates of change in coverage of health services can be estimated empirically (eg, by taking the first derivative of coverage), but their evolution over time can also be captured by mathematical models, including simple ordinary differential equations such as growth curves. Indeed, growth curves have been used in numerous other academic disciplines to model specific dynamic phenomena, and they could yield meaningful summary parameters that characterise intervention scale-up. For example, in telecommunications, the Bass diffusion equation models the spread of innovation or adoption of new technologies in a population\(^\text{17}\); and in cell biology, growth curves can be used to represent bacterial growth.\(^\text{18}\) Despite these common uses, such differential equation models have not been widely implemented in global public health.

Growth curve models could parameterise and capture the evolution of health services coverage over time. In this paper, we illustrate the relevance of growth curves by attempting to characterise and parameterise the growth in antiretroviral therapy (ART) coverage in 42 sub-Saharan African countries using two long-established growth models: the logistic and the Gompertz models. We then extract summary metrics (eg, rate of scale-up, time delay to scale-up) that describe the evolution of ART coverage and thus may be of use to analysts interested in understanding cross-country variation in ART coverage evolution in sub-Saharan Africa.

### METHODS

#### Data sources

We used country-level data on ART coverage from 2000 to 2017 from the World Bank’s World Development Indicators database; these data were originally sourced from UNAIDS estimates.\(^\text{19}\) ART coverage is defined as the percentage of people living with HIV who are receiving ART; the numerator (ie, the number of people on ART) is aggregated at the country level, and UNAIDS models generate the denominator (ie, the population living with...
HIV).\textsuperscript{20–22} We limited our analysis to sub-Saharan Africa, the region most impacted by HIV: according to UNAIDS, it accounted for close to 70% of all people living with HIV in 2018.\textsuperscript{23} We further limited our analysis to countries with a population exceeding one million,\textsuperscript{24} leading to a sample of 42 sub-Saharan African countries.

**Mathematical approach**

We used two types of ordinary differential equations to model the growth in ART coverage over time in the selected countries: the logistic and the Gompertz equations (table 1). In their canonical forms, these models are not easily interpretable in a global health context.\textsuperscript{18} Therefore, we used the transformations described by Zwietering \textit{et al} for both the Gompertz and logistic equations.\textsuperscript{18} The derived parameters (see ‘modified solutions’) have an intuitive interpretation: \(A\) represents the projected maximum level of intervention coverage (in percentage points); \(\mu\) the maximum growth or maximum scale-up rate of intervention coverage (in percentage points per year); and \(\lambda\) the lag or delay time prior to the start of the intervention implementation (in years). The initial level of intervention coverage is represented by \(y_0\) (figure 1 provides a graphical representation).

The logistic equation is a simple and widely used growth curve model. Though its simplicity is advantageous, it may not be well suited to model coverage scale-up and evolution, especially since it is symmetric in shape. The maximum growth rate (ie, the slope at the inflection point of the coverage curve) occurs halfway between the initial value (\(y_0\)) and the asymptotic carrying capacity (\(A\)). There is no a priori reason to believe that growth in ART coverage over time would be symmetric or that the highest rate of growth would be exactly halfway between these two points (ie, the start and end points). Unlike the logistic equation, the Gompertz equation allows for asymmetry, as the maximum growth rate need not occur exactly halfway between \(y_0\) and \(A\). This property may better fit with the study of ART coverage evolution over time: coverage may grow rapidly in the initial stages of a programme, but marginal gains in later stages may be
We first display the fits of the Gompertz and logistic growth models to the data of six selected sub-Saharan African countries (figure 2), along with the estimated maximum rates of change (rates of scale-up, denoted μ) across all the countries examined (figure 3).

With the Gompertz growth curve, across all countries in the sample, the mean value of μ was 5.1 percentage points per year, with a range from 1.3 percentage points per year (Sudan) to 9.5 percentage points per year (Benin). For the logistic growth curve, estimates of μ ranged from 1.5 percentage points per year (Sudan) to 10.0 percentage points per year (Benin), with a mean value of 5.8 percentage points per year. Country-specific estimates from the Gompertz and logistic growth models tended to cluster near similar values (figure 3). Still, there were a few countries where estimates of μ diverged. For example, for Madagascar, the Gompertz growth model estimated μ=2.5 percentage points per year, whereas the logistic growth model estimated μ=6.5 percentage points per year; for Sierra Leone, 4.5 percentage points per year for the Gompertz versus 7.0 for the logistic. However, Madagascar and Sierra Leone stand out as singular cases as both countries have relatively low HIV prevalence (0.3% and 1.5% of the adult population, respectively25); and Madagascar had ART coverage levels below 10%, which thus makes it difficult to model ART coverage scale-up given the relatively low changes in coverage magnitude over time.

Table 2 shows the estimated rates of change per country along with an associated ranking. For a majority of countries, the rankings were similar across Gompertz versus logistic growth curves. For example, Benin remained a top performer, while Sudan remained a bottom performer. In between, however, the rankings were less stable. For example, when examining the observed crude average rate of change over the 2000–2017 time period (defined as current ART coverage divided by the number of years since ART coverage >0), Benin ranked 18th, while it ranked 1st under the observed μ for the logistic growth model; Botswana ranked 2nd under the observed μ; and Benin ranked 1st under the estimated μ from the logistic growth model. Overall, correlation of ranks on μ across all countries in the sample of 0.94 between the logistic and Gompertz models; 0.87 between Gompertz’s μ and the observed crude average rate of change; and 0.79 between logistic’s μ and the observed crude average rate of change. These differences also come from the fact that average rates of change (over the entire 2000–2017 time period) and maximum rates of change capture two different coverage evolution phenomena.

As for time delays, the estimated mean value (across all countries in the sample) of λ was 6.5 years with the Gompertz growth model compared with 7.3 years with
Table 2  Estimated maximum rate of change in antiretroviral therapy (ART) coverage (denoted $\mu$, maximum estimated rate of scale-up in percentage points per year) for 42 sub-Saharan African countries, and corresponding ranks (across all countries in the sample), for the Gompertz and logistic models

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The ‘observed crude average change’ (2017 ART coverage divided by the number of years since ART coverage >0) displays the observed crude average rate of change over the entire 2000–2017 time period.
In evaluating the goodness of fit of each growth model, we sought the model with the lowest BIC. For this comparison, across countries, we subtracted the BIC of the logistic growth model from the BIC of the Gompertz model, and calculated ΔBIC. When ΔBIC > 6, the logistic growth model would be supported; when ΔBIC < < 6, the Gompertz growth model would be supported. Our findings were then split between the two models, with the Gompertz model generally providing a better fit for most countries. Differences in BIC ranged from 22 for Uganda to −26 for Malawi (figure 5).

DISCUSSION

In this paper, we used two simple and intuitive differential equations, the logistic and the Gompertz growth curves, to characterise changes in ART coverage over 2000–2017 for 42 sub-Saharan African countries. Using nonlinear regressions, we estimated key parameters to describe ART coverage evolution, including the maximum rate of change (μ in percentage points per year) and the lag time to coverage scale-up (λ in years). We were then able to compare these estimated parameters to observed ART coverage data to describe how ART performance and scale-up varies across sub-Saharan African countries.

Some countries performed consistently well across growth models. For example, Botswana was the highest ranking country across all estimated parameters for the time delay in ART scale-up (λ), and also ranked well for its estimates in maximum rates of change of scale-up (μ). This reflects the success Botswana achieved in scaling up its ART programme. Since 2002, Botswana has committed significant resources to establishing universal coverage for ART; consequently, mortality among people living with HIV in the country fell dramatically. Likewise, Rwanda is another success story highlighted here; it ranks fifth in the estimated delay in ART scale-up (4.3 years with the Gompertz model) and fourth in the estimated maximum rate of change (7.5 percentage points per year, with the Gompertz model). Although few people living with HIV were being treated back in 2003, the country had already achieved, by 2017, ART coverage levels greater than 80%. On the contrary, South Africa demonstrated a significant delay in ART scale-up (around 6–7 years as estimated by each growth model), consistent with the evolution of national ART coverage and the postponing of ART scale-up in the country. After 2006, when ART coverage was then at 4%, South Africa significantly grew its ART programme and achieved rapid coverage expansion of approximately 1.8 million people by 2011 and over 3 million people by 2017, for a current ART coverage of about 61%. Therefore, our growth models and their estimates of maximum rates of change and time delays could provide analysts with useful summary indicators for characterising the evolution over time of key health services (ART in our case study here).

Nevertheless, our analysis presents a number of limitations. First, our approach cannot be generalisable as we...
Table 3  Estimated time delay in antiretroviral therapy (ART) coverage scale-up (denoted $\lambda$ in years) for 42 sub-Saharan African countries, and corresponding ranks (across all countries in the sample), for the Gompertz and logistic models

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The ‘observed crude’ time delay corresponds to the lag time calculated as the number of years between 2000 and a country’s first year with ART coverage >0.
have only tested it with time series data on ART coverage in sub-Saharan Africa. It is important to note that until recently, patients would only receive ART after meeting certain eligibility criteria (eg, CD4 cell counts), and that patients who did not meet these criteria would wait to receive ART. Additionally, although ART may be important in tackling the AIDS epidemic, there are other health services that could be studied for addressing HIV/AIDS. Most importantly, the scale-up of ART programmes could differ from the provision and scale-up of general health services; for example, general health services may be more freely accessible and/or depend less on development assistance. However, when applied to relevant health services indicators, growth curve models could be adapted to analyse progress in other disease areas and conditions (eg, introduction of a new drug or new vaccine).

Second, our time series coverage data may also be subject to correlations between countries and within country, and one could potentially refine the statistical modelling by introducing country-specific and time-specific random effects. Although an estimated rate of change (μ) and estimated time delay (λ) may be useful to summarise intervention scale-up evolution, they are merely two simple indicators: many factors influence intervention scale-up, and thus μ and λ can in no way answer the fundamental question of why a country might perform well or poorly in one of its programmes; μ and λ likely encapsulate many parts of a complex health system architecture, which requires further in-depth investigation.

Third, the UNAIDS ART coverage data used for this analysis were themselves derived from modelled estimates, such as country-specific numbers of people living with HIV. Although these models estimate lower and upper limits of uncertainty, we chose to fit our models to the best estimates of ART coverage. By fitting regression models in this way, we may compound their inherent uncertainty. Also, the ART coverage data could be rounded to the nearest whole number, which would lead to complications in the interpretation of our estimated country-specific time delays. Finally, the first year of non-zero ART coverage might reflect data collection practices rather than the true start of programme implementation. Due to these sources of uncertainty, we emphasise the potential utility of these performance evaluation methods, and would advise caution when interpreting our results against the actual state of ART care in sub-Saharan Africa.

Fourth, our growth models did not incorporate any information on specific country contexts. In some countries, such as Burkina Faso and the Democratic Republic of the Congo, less than 1% of the population suffer from HIV; this may explain some of the poor regression fits, for either one or both of the growth models. In contrast, adult prevalence of HIV is near or above 20% in South Africa, Swaziland and Botswana. Clearly, the latter group of countries faces different challenges to HIV management and ART scale-up than the former. Lastly, since the structure of health financing can differ significantly across countries, differences in the structure of ART programmes across countries could reflect this heterogeneity as well.

In summary, our growth models were purposely simple and non-mechanistic (eg, no inclusion of HIV transmission dynamics) as they did not rely on existing frameworks for health system analysis. Notably, the information gleaned from our modelling approach should be augmented with the economic and historical context of a given country. As Balabanova et al point out, the ability of a health system to scale-up an intervention (ie, to achieve a high rate of change or a low lag time) is influenced by the system’s history and development. Our objective in this paper is to present a simple approach to estimate meaningful parameters that can summarise health services scale-up, which may be a useful step towards characterising and understanding performance of national disease-specific programmes.

To conclude, our analysis intends to contribute to the growing acknowledgement that rates of change in health outcomes and health services coverage may provide helpful insight into the understanding of country performance on health. Although they are only a starting point, growth curves and basic differential equation models can provide a novel perspective on the scale-up of key interventions in global health.

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manuscript. Both authors critically revised the content of the paper, approved the final version and agree to be accountable for all aspects of the work.

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Competing interests BB is currently employed by Hospital IQ (Newton, MA), a healthcare software company. As part of his employment package, BB has received stock options from Hospital IQ; BB also owns stock in CareJourney (Arlington, VA), another healthcare software company. The majority of research, data analysis, and manuscript preparation occurred while BB was at Harvard University, prior to his employment at Hospital IQ. SV has no conflicts of interest to declare.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. Data are available upon reasonable request. All source data are publicly available from the World Bank: https://data.worldbank.org/. The data and code for the analysis can be accessed from the manuscript’s GitHub repository: https://github.com/bbigelow/growth-curves.

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