

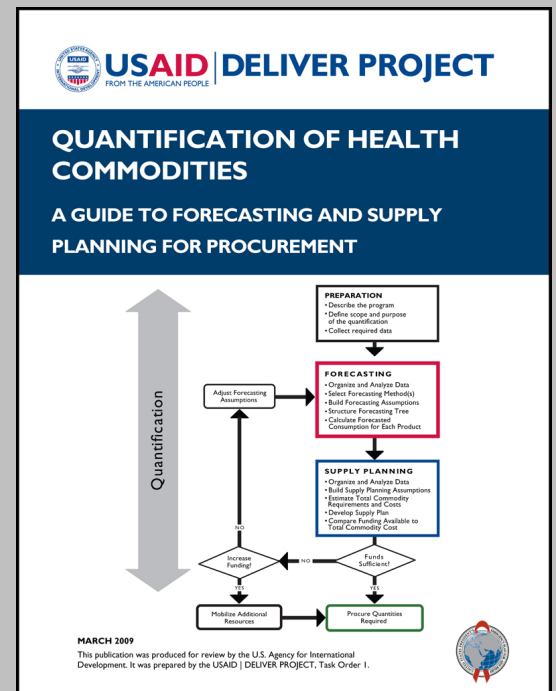


QUANTIFICATION OF HEALTH COMMODITIES: ARV COMPANION GUIDE

Forecasting ARV Drugs Using the Morbidity Method



To be used in conjunction with:



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QUANTIFICATION OF HEALTH COMMODITIES: ARV COMPANION GUIDE

Forecasting ARV Drugs Using the Morbidity Method

USAID | DELIVER PROJECT, Task Order 1

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Abstract

Successful implementation and expansion of antiretroviral therapy (ART) services depend on the continuous availability of high-quality antiretroviral (ARV) drugs and on the supply of a wide range of HIV & AIDS-related commodities. The nature of ART and the specific characteristics of ARV drugs and how they are used pose particular challenges for managing the supply chain for ARV drugs. The primary focus and purpose of the ARV companion guide is to describe the process and the methods used for forecasting ARV drug needs.

Cover photo: A pharmacist dispenses ARVs.

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CONTENTS

- Acronyms..... v
- Introduction to ARV Drug Forecasting..... 1
 - How to Use This Companion Guide..... 1
- Characteristics of ARV Drugs 3
- Steps in Forecasting ARV Drug Consumption Using the Morbidity Method 7
 - Collect Required Data..... 8
 - Organize and Analyze the Data..... 12
 - Build the Forecasting Assumptions 13
 - Create a Forecasting Tree..... 14
 - Calculate Forecasted Consumption for Each Product: Step by Step..... 15
- Considerations for Forecasting Pediatric ARV Drugs 17
- Summary of Challenges and Lessons Learned in Quantification of ARV Drugs..... 23
 - Common Challenges..... 23
 - Lessons Learned..... 24
- References 25
 - Additional Relevant Documents or Country Reports..... 25

Tables

- 1. Common ARV Drugs (Adults and Children)..... 4
- 2. Examples of Fixed Dose Combination Drugs (Illustrative List Only) 5
- 3. Examples of Common ARV Drug Regimens (Illustrative List Only)..... 6
- 4. Country Example: Key Programmatic Issues Affecting the Forecast..... 10
- 5. Organizing Data for the Forecast..... 12

Figures

- 1. Steps in Quantification 1
- 2. Forecasting Tree..... 15

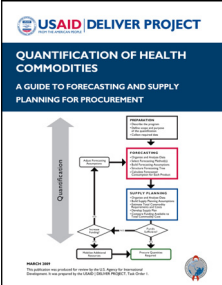
ACRONYMS

3TC	lamivudine
ABC	abacavir
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral
AZT	zidovudine
ddI	didanosine
d4T	stavudine
EFV	efavirenz
FDC	fixed dose combination
FTC	emtricitabine
HBC	home-based care
HIV	human immunodeficiency virus
LMIS	logistics management information system
LPV/r	lopinavir + ritonavir
NACP	National AIDS Control Program
NVP	nevirapine
PEP	post-exposure prophylaxis
PMTCT	preventing mother-to-child transmission
SQV	saquinavir
STGs	standard treatment guidelines
TB	tuberculosis
UNAIDS	Joint United Nations Programme on HIV/AIDS
USAID	U.S. Agency for International Development
WHO	World Health Organization
ZDV	zidovudine

INTRODUCTION TO ARV DRUG FORECASTING

Successful antiretroviral therapy (ART) programs depend on uninterrupted patient adherence to prescribed antiretroviral (ARV) drug regimens and on maintenance of a full supply of ARV drugs at ART sites. The threat of drug resistance and changes in patients’ responses to treatment over time make it imperative to ensure an uninterrupted supply of quality ARV drugs that respond to patient needs and that are available when and where patients need them. To achieve these goals, the ARV drug supply chain must accommodate the specific characteristics of ARV drugs, the ways they are used, and special requirements for their storage and handling. This knowledge must be incorporated into the quantification of needs to ensure procurement of the right quantities of the right drugs.

HOW TO USE THIS COMPANION GUIDE

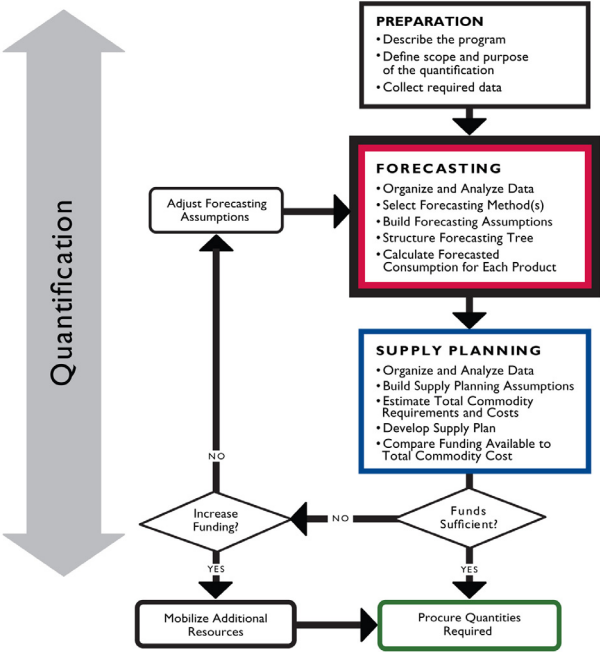


This companion guide is intended to complement information on the preparation and supply planning steps in the *Quantification of Health Commodities: A Guide to Forecasting and Supply Planning for Procurement* (the main guide). The main guide provides information on how to conduct consumption-based forecasts for all commodity categories. This companion

piece provides specific instructions **for using the morbidity method to forecast ARV drug requirements** and follows an actual ARV forecasting exercise using the morbidity method. The instructions include input data and assumptions specifically required for an ARV morbidity-based forecast. They also outline what the outputs should be with specific examples from an actual national ART program forecast.

This document also provides information specific to ARV drugs themselves. After completing the forecasting step using this ARV companion guide, users should refer to the main guide to compare the outputs from the different forecasting methods and complete the supply planning step of the quantification to obtain the final outputs (see figure 1).

Figure 1. Steps in Quantification



CHARACTERISTICS OF ARV DRUGS

Forecasts using the morbidity method rely on translating numbers of patients and services into quantities of drugs used. It is important to understand the characteristics of ARV drugs and the context in which they are prescribed in order to produce an accurate forecast. Typically, ARV drug regimens consist of three drugs. The initial use of those regimens is influenced by patients' previous ARV drug history, other co-existing infections or conditions, provider prescribing patterns, drug supply, and other factors. The drugs within a regimen must be adjusted over time to capture the changing needs of patients that are caused by side effects and toxicities to individual drugs, changing body weight, pregnancy, human immunodeficiency virus (HIV)/tuberculosis (TB) co-infection, treatment failure, and drug resistance. Forecasts may also need to account for patients on nonstandard ARV drug regimens who may have entered the program already on ART, as well as patients who are on individualized salvage therapy.

ARV drugs have several characteristics that affect the management of the commodities and that pose unique challenges in quantification. Those characteristics include, but are not limited to, the following:

- ART requires lifelong treatment.
- A single ARV drug regimen requires a combination of at least three different drugs, often from different manufacturers, to be available concurrently.
- Each drug is often used in more than one regimen.
- The choice of regimens includes considerations of weight and toxicity, factors unique to individual patients. For most programs, data on these individual patient characteristics and factors are not being captured and cannot be utilized for forecasting. This unpredictability is particularly true for pediatric patients, for whom changes in weight vary significantly even within a population and body surface is a factor in calculating dosage.
- Treatment failure is difficult to predict and to diagnose in resource-poor settings.

ARV drugs have varying dosages and formulations to accommodate individual patient needs. For example, table 1 lists common ARV drugs and shows that didanosine is available in as many as 10 formulations for adults and pediatric patients.

Table 1. Common ARV Drugs (Adults and Children)

Adult and Adolescent Formulations	Pediatric Formulations
<i>Nucleoside Reverse Transcriptase Inhibitors</i>	
abacavir (ABC) 300 mg tablet	abacavir (ABC) oral solution, 20 mg/ml bottle
didanosine (ddl) 125 mg, 200 mg, 250 mg, and 400 mg enteric-coated capsule	didanosine (ddl) 25 mg, 50mg, 100 mg, 150 mg, and 200 mg chewable tablet didanosine (ddl) oral suspension, 10 mg/ml bottle
lamivudine (3TC) 150 mg tablet	lamivudine (3TC) oral solution, 10 mg/ml bottle
stavudine (d4T) 15 mg, 20 mg, 30 mg, and 40 mg capsule	stavudine (d4T) oral solution, 1 mg/ml bottle
zidovudine (AZT or ZDV) 100 mg and 250 mg capsule, 300 mg tablet	zidovudine (AZT or ZDV) syrup, 10 mg/ml bottle
emtricitabine (FTC) 200 mg capsule	
<i>Nucleotide Reverse Transcriptase Inhibitors</i>	
tenofovir (TDF) 300 mg tablet	
<i>Nonnucleoside Reverse Transcriptase Inhibitors</i>	
efavirenz (EFV) 50 mg, 100 mg, and 200 mg capsule	
efavirenz (EFV) 600 mg tablet	
nevirapine (NVP) 200 mg tablet	nevirapine (NVP) oral suspension, 10 mg/ml bottle
<i>Protease Inhibitors</i>	
indinavir (IDV) 100 mg, 200 mg, 333 mg, and 400 mg capsule	
lopinavir + ritonavir (LPV/r) 133.3 mg/33.3 mg capsule	
lopinavir + ritonavir (LPV/r) 80 mg/ml + 20 mg/ml oral solution	
saquinavir (SQV) 200 mg soft gel capsule, 200 mg hard gel capsule	
ritonavir 100 mg capsule, 80 mg/ml oral solution	

Many common ARV drug regimens are available as fixed dose combination drugs (FDCs); however, single-drug formulations must be available for substitution within first and second line regimens because some patients develop side effects or toxicity to individual drugs, and because three completely different ARV drugs for second line regimens must be available for patients who develop resistance to first line drugs. Table 2 lists some common examples of FDC ARV drugs. Specific formulations for pediatric treatment regimens include oral suspensions (syrups), chewable and dispersible FDCs, and children’s dosages of tablets and capsules, which are adjusted for weight and body surface area measurements.

Table 2. Examples of Fixed Dose Combination Drugs (Illustrative List Only)

Examples of Fixed Dose Combination Drugs
stavudine 30 mg + lamivudine 150 mg + nevirapine 200 mg tablet (d4T30/3TC/NVP)
zidovudine 300 mg + lamivudine 150 mg tablet (AZT/3TC or ZDV/3TC)
zidovudine 300 mg + lamivudine 150 mg + abacavir 300 mg tablet (ZDV/3TC/ABC)
tenofovir 300 mg + emtricitabine 200 mg tablet (TDF/FTC)

A country's forecasts need to be updated routinely (ideally quarterly, but at least semi-annually) to accommodate new ARV drug formulations and more user-friendly fixed dose combinations as they become available. More information on suppliers, packaging, storage, shelf life, and pricing of these and other ARV drugs is available from *Logistics Fact Sheets: ARV Drugs* (USAID | DELIVER PROJECT 2008) and the Partnership for Supply Chain Management e-catalog available at the project website: <http://scms.pfscm.org/scms/ecatalog>. The World Health Organization's publication entitled *Scaling Up Antiretroviral Therapy in Resource-Limited Settings: Treatment Guidelines for a Public Health Approach* (WHO 2003) has additional information on adult and pediatric dosing regimens and on prescribing guidelines. These guidelines are regularly updated by WHO to reflect current circumstances. Readers should refer to in-country standard treatment guidelines and other sources for up-to-date information on which drugs are available and approved for use in particular countries.

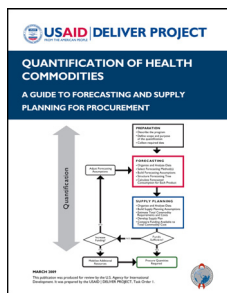
National ART guidelines generally include standard first line and second line treatment regimens for adults and children, regimens for preventing mother-to-child transmission (PMTCT), and treatment for patients with HIV/TB co-infection and for post-exposure prophylaxis (PEP). Frequently, national quantifications will include forecasting demand for all uses of ARV drugs as part of the overall requirements estimation. The specific uses of ARV drugs to be included in the forecast should be clearly identified as part of the preparation phase of the quantification.

Table 3 is a list of common ARV drug regimens. It illustrates how a single drug may be used in several different regimens. For example, in the table, lamivudine (or 3TC) is used in all of the adult and pediatric first line regimens, and didanosine (or ddI) is used in half of the adult and all of the pediatric second line regimens.

Table 3. Examples of Common ARV Drug Regimens (Illustrative List Only)

Adult First Line Regimens	Adult Second Line Regimens	Pediatric First Line Regimens	Pediatric Second Line Regimens	PMTCT	Post-exposure Prophylaxis
d4T + 3TC + NVP	ddl + 3TC + LPV/r	d4T + 3TC + NVP	ddl + ABC + LPV/r	ZDV + 3TC (mother)	High-risk exposure ZDV + 3TC + IDV
d4T + 3TC + EFV	TDF + 3TC + LPV/r	d4T + 3TC + EFV	ddl + ZDV + LPV/r	ZDV + 3TC (infant)	Low-risk exposure ZDV + 3TC
ZDV + 3TC + NVP	ddl + ABC + LPV/r	ZDV + 3TC + NVP	ddl + EFV + LPV/r		
ZDV + 3TC + EFV	TDF + ABC + LPV/r	ZDV + 3TC + EFV		NVP 200 mg tablet (mother)	
TDF + 3TC + NVP				NVP 10 mg/ml syrup (infant)	
TDF + 3TC + EFV					

STEPS IN FORECASTING ARV DRUG CONSUMPTION USING THE MORBIDITY METHOD



In general, the method selected for forecasting consumption of ARV drugs needs is based on the availability and quality of consumption, services, morbidity, and demographic data.

This companion piece guides users through the steps in forecasting ARV drug consumption using the morbidity method. The morbidity method uses morbidity, services, or demographic data to estimate the number of people or episodes of a disease that are expected to be treated, and then translates these into the number of products expected to be consumed. Consult *Quantification of Health Commodities:*

A Guide to Forecasting and Supply Planning for Procurement, the main guide for this companion piece, for information on the different types of data used for forecasting and the two forecasting methods: morbidity and consumption. It is recommended to conduct multiple forecasts using as many data sources as possible. The use of historical consumption data is the best predictor for future consumption when programs are stable. However, because consumption data are not always available and are not predictive of future consumption when services are scaling up or when products change, the morbidity method should be utilized.

A number of steps in the quantification process must be completed before collecting data and forecasting consumption. These steps include selecting the quantification team, describing the program, and defining the scope, purpose, and timeframe of the quantification.

Country Example: Background

The Ministry of Health wanted to conduct a quantification for all ARV drug requirements for public sector facilities from January 2009 to December 2010. The ARV drug needs were to include the needs for ART, PMTCT, and PEP. The quantification was to include the total cost estimate per year for procurement and to identify any funding gaps that needed to be addressed. The quantification team was composed of logistics advisors, staff from the National AIDS Control Program (NACP), and two technical advisors from the project. Four weeks were allotted for the completion of this exercise.

COLLECT REQUIRED DATA

Collecting required data is part of the preparation step in the quantification process. The data that are listed here are specific for conducting a morbidity-based forecast using service, morbidity, or demographic data.

Data for Forecasting

Specific data on the number and type of health services provided may be collected through existing health management information system (HMIS) and logistics management information system (LMIS) reports and through direct data collection at health facilities. Data may also be obtained through interviews with central-level and facility-level staff, as well as from review of key policy documents, technical reports, national surveillance reports, and special studies.

Country example: Data sources:

- Several types of data (services, epidemiological, national ART guidelines, targets, etc.) provided by the NACP
- Technical reports on earlier ARV drug quantifications
- Consultative interviews and discussions with central-level stakeholders including the NACP, nongovernmental organizations, and care and treatment partners
- Aggregated and facility services data on the number of patients on ART by regimen provided by U.S. government partners
- Nine facility visits to collect data and interview staff

The specific data below should be collected:

1. A list of all ARV drug regimens used in the program and that will continue to be used

Country example: Adult ART regimens included in the forecast:

- d4T/3TC/NVP
- d4T/3TC + EFV
- AZT/3TC + NVP
- AZT/3TC + EFV
- TDF/FTC + NVP
- TDF/FTC/EFV
- ABC + ddI 250 + LPV/r
- ABC + ddI 400 + LPV/r
- ABC + TDF + LPV/r

2. A list of stockkeeping units used in the program (and that the program would like to continue to use)

Country example: Adult ARV drugs included in the forecast:

- 3TC 150 mg tablets
- ABC 300 mg tablets
- AZT 300 mg tablets
- AZT/3TC 300/50 mg tablets
- NVP 200 mg tablets
- d4T/3TC 30/150 mg tablets
- d4T/3TC/NVP 30/150/200 mg tablets
- ddl 100 mg tablets
- ddl 200 mg tablets
- ddl 250 mg capsules
- ddl 400 mg capsules
- EFV 200 mg capsules
- EFV 600 mg tablets
- LPV/r 200/50 mg tablets
- TDF/3TC 300/200 mg tablets

3. Demographic and population data: Total population numbers and growth, demographic trends. These data may also include the population breakdown of adults and children.

Country example: Demographic data

These data were obtained from World Health Organization (WHO)/Joint United Nations Programme on HIV & AIDS (UNAIDS) estimates:

- Total population: 40,454,000
- Population aged 15–49: 18,734,000
- Annual population growth rate: 1.8%

4. Morbidity data: Prevalence of HIV and, if available, acquired immunodeficiency syndrome (AIDS) (may be available by population group, through surveillance or study group, and extrapolated to estimate national-level incidence and prevalence of HIV)

Country example: Morbidity data

These data were obtained from WHO/UNAIDS estimates

- Adult HIV prevalence rate: 6.1%
- Number of adults living with HIV: 1,300,000
- Number of children living with HIV: 140,000

- Services data: Number of patients receiving ART over the past 12-month period, and the number of new patients started each month. The number of patients on treatment should be reported by regimen.

Country example: Services data: Total number of patients receiving ART

These data were obtained from the NACP and from U.S. government care and treatment partners. As of December 2008, there were—

- 102,769 adults on first line treatment
- 1,038 adults on second line treatment
- 11,419 pediatric patients on first line treatment
- 115 pediatric patients on second line treatment

- Information on current program performance, plans, strategies, and priorities including specific program targets, and numbers of patients targeted to be on ART for each year of the forecast (see table 4).

Table 4. Country Example: Key Programmatic Issues Affecting the Forecast

Issue	Effect on Forecast
<p>National ART Guidelines had recently been reviewed and changed, and were pending official approval. Changes included</p> <ul style="list-style-type: none"> • new adult first line regimens (TDF + 3TC + NVP, TDF + 3TC + EFV) • new adult second line regimens (ABC + TDF + LPV/r) 	<p>Need to determine whether new adult regimens are for new patients, or whether existing patients will be switched to these regimens.</p> <p>Need to determine when the guidelines will be implemented, when clinicians and site-level staff will be trained, and verify that information on new products is accounted for into the LMIS. If drugs are procured too early and program staff have not been trained on how to use them, the LMIS does not include them and it is likely that products will sit at the warehouse and not be distributed to sites.</p>
<p>Shift from standard first line regimen from d4T/3TC/NVP to AZT/3TC + EFV</p>	<p>Need to determine whether existing patients on d4T/3TC/NVP will be switched to AZT/3TC + EFV or if only new patients will be started on that regimen.</p>
<p>New drug formulations would also be available:</p> <ul style="list-style-type: none"> • switch from ddl 100 mg tablets to ddl 400 mg enteric-coated capsules • introduce dispersible fixed dose combinations of d4T/3TC/NVP for pediatric patients 	<p>Need to determine when the guidelines will be implemented, when clinicians and site-level staff will be trained, and verify that information on new products is accounted for into the LMIS. If drugs are procured too early, and program staff have not been trained on how to use them, the LMIS does not include them and it is likely that products will sit at the warehouse and not be distributed to sites.</p>
<p>New regimens for PMTCT are in the process of being implemented.</p>	<p>Need to determine the exact regimens, and drugs that comprise the regimens. Also need to determine the national roll-out plan for the implementation of these new regimens.</p>
<p>Government plans to scale up number of sites from 237 to 700 within the first year of the quantification.</p>	<p>Need to determine how realistic this scale-up rate is. Have the existing facilities reached their capacity? Will the scale-up rates at the new facilities be greater than</p>

Issue	Effect on Forecast
ARV drug logistics system had recently been redesigned, including revised LMIS records and reports.	<p>the scale-up rates at existing facilities?</p> <p>Shows that the program is going through a major transition in terms of logistics, and that national-level consumption and stock on hand information will not be available until after the system has been rolled out nationally.</p>
Official government target for numbers on ART at the end of 2009 was 300,000.	Need to determine how realistic this figure is given past scale-up rates, current numbers of patients on treatment, available funding, and existing capacity.

ORGANIZE AND ANALYZE THE DATA

One of the most critical steps for the quantification team is to assess the quality of the data to determine if the data can be used for the quantification. The data collected were organized into a table for analysis (see table 5).

Table 5. Organizing Data for the Forecast

Type of Data	Data	Quality of Data	Notes
Services	Total number of patients on ART e.g., 102,769 adults on ART	Facility reporting rate is 67%	Includes the cumulative number of patients that ever started ART since October 2004, when services began. Does not account for any patients that have discontinued treatment.
	Number of patients on ART by regimen e.g., 44,190 adults on d4T/3TC/NVP	Collected at 9 facilities and from individual partners supporting facilities.	Newly revised ART patient registers collect the number of patients by ART regimen, but data are not being reported or aggregated at the central level.
Target	National program targets for 2009 and 2010. e.g., 300,000 is target number of ART patients for 2009	Not based on existing patients or historical scale-up rates	Not used for the forecast
Consumption	Quantities of ARV drugs issued to facilities over the past 12 months e.g., 650,000 bottles of d4T/3TC/NVP	Consumption data not available. Issues data used as proxy for consumption.	Not used for the forecast
	Central-level stock on hand e.g., 700,000 bottles of d4T/3TC/NVP on hand	Facility-level stock on hand not available	Used for the supply planning step. See main guide for more information.
Morbidity	HIV prevalence rate e.g., Adults: 6.1%	1 year old	Not used for the forecast
Demographic	Total population e.g., 40,454,000 Population growth rate Population aged 15–49	1 year old	Not used for the forecast

After all the historical data are evaluated and adjusted, the quantification team should formulate and obtain consensus on assumptions about future program growth and to account for any missing, incomplete, or poor-quality data.

BUILD THE FORECASTING ASSUMPTIONS

Assumptions need to be made to account for missing or incomplete data and to estimate the effect of key programmatic and environmental factors expected to influence the demand for ARV drugs for each year of the forecast. Consensus must be obtained on the assumptions.

The following are examples of programmatic and environmental factors that may affect demand for services and commodities and may need to be taken into account in the forecasting assumptions.

- Changes in standard treatment guidelines (STGs) mandating product selection and how products are to be prescribed whereby instant policy change does not immediately reflect the change in prescribing behavior (usually requires training of providers and takes six months or more to be fully implemented)
- Emergence of new products and formulations on the market
- Changes in program priorities, strategies, and goals, particularly targets for coverage (e.g., pediatric ART, ART lab diagnostics and monitoring, increased focus on home-based care (HBC) and nutritional support), that result in demand for new ARV drugs or may create variation in consumption of existing ARV drugs
- Changes in political, legal, or regulatory environment (e.g., introduction of ARV drugs being provided free of charge)
- Societal and behavioral factors (e.g., reduction in stigma affects demand for ARVs)

Country Example: Assumptions

- Because of the time required for training service providers, implementing the new ART guidelines, and procurement lead times, the new ARV drug regimens (including the new drugs) and new formulations of ARV drugs as recommended in the revised guidelines will not be distributed and utilized at facilities until year 2 of the quantification.
- A default rate of 10% will be applied to total ART patients for each year of the forecast. This applies to both existing patients and new patients.
- Proportion of total patients on ART that are adults (90%) vs. children (10%)
- Percentages of patients on first line treatment (99%) and second line treatment (1%)
- Within each treatment category (first line or second line), the percentages of patients on each nationally prescribed first and second line treatment regimens (i.e., d4T/3TC/NVP)
- On the basis of historical growth rates (scale up from January to December 2008), at the end of year 1 of the quantification period, a total of 189,187 patients would be on treatment. At the end of year 2, there would be 259,528 patients.
- The increase of patients would be steady through each month, with a net of 6,154 patients added each month during year 1 and 5,862 patients added each month during year 2.

CREATE A FORECASTING TREE

For forecasts using the morbidity method, a forecasting tree should be constructed to organize and use the data and assumptions to help estimate future consumption. The forecasting tree is a diagram of patient groups (or health conditions) and the products required to treat one patient or one episode. It can be completed with a pencil and paper (no software is needed). Data required to conduct a forecasting tree are—

- STGs (treatment regimens)
- specific patient groups or health conditions
- list of products and specific product characteristics (e.g., formulations and dosages and pack sizes).

Steps for constructing a forecasting tree are as follows:

1. Identify the specific disease or health condition for which the commodities are to be forecasted.

Country example: Health condition Antiretroviral therapy

2. Separate the logical patient groups or health conditions to be treated, and assign the percentages for each patient group. For ARV drugs, the patient groups could be adults vs. children further separated into the subgroups first line vs. second line. Patient groups could also be formed for PEP and PMTCT.

Country example: Patient groups Adults, children

These are further divided into adults on first and second line regimens, and children on, first and second line regimens.

3. For each of the patient groups, list all the possible treatment regimens for each group and the percentage of patients that will be on each regimen.

Country example: Regimens

Adult first line regimens:

- d4T/3TC/NVP
- d4T/3TC + EFV
- AZT/3TC + NVP
- AZT/3TC + EFV
- TDF/FTC + NVP
- TDF/FTC + EFV

Adult second line regimens:

- ABC + ddI250 + LPV/r
- ABC + ddI400 + LPV/r
- ABC + TDF + LPV/r

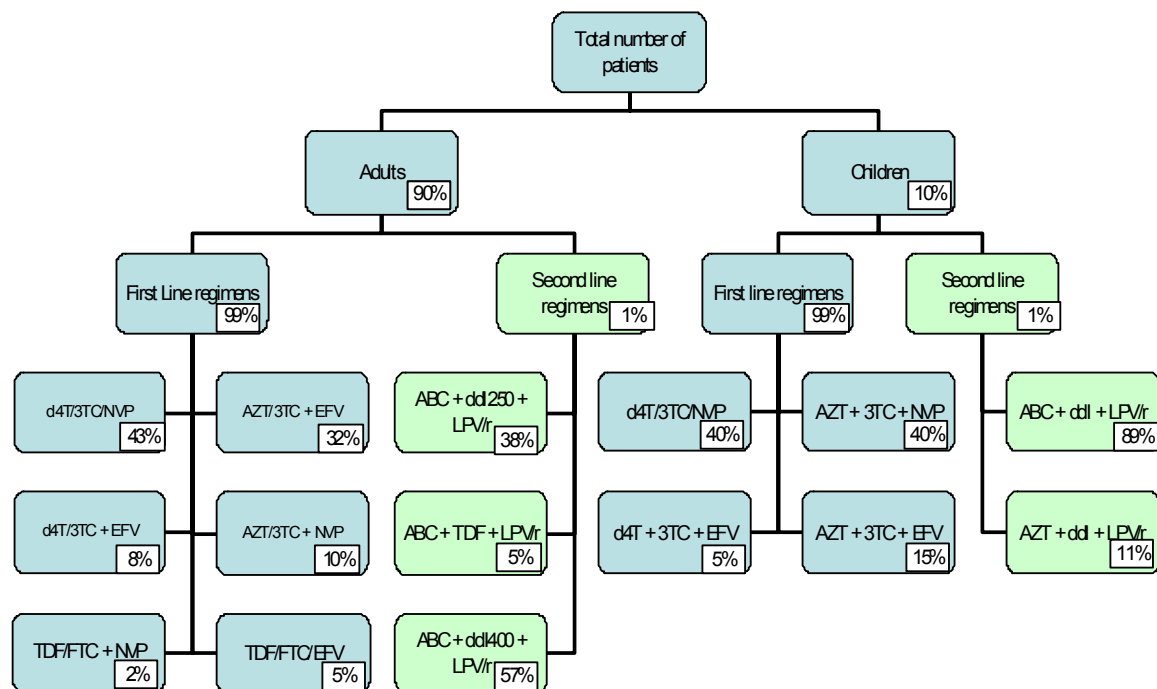
- Assign the specific drugs required for each of the possible treatment regimens within each patient group.

Country example: Drugs

Adults on the regimen AZT/3TC + NVP will receive 2 tablets daily of the FDC AZT/3TC and 2 tablets daily of single formulation NVP.

See figure 2 for a sample forecasting tree for year 1 of the quantification. If changes in STGs between year 1 and year 2 of the quantification are anticipated, then a forecasting tree must be created for each year of the forecast.

Figure 2. Forecasting Tree



CALCULATE FORECASTED CONSUMPTION FOR EACH PRODUCT: STEP BY STEP

After the forecasting tree is completed and the number of patients expected to be on each regimen for each month and year of the forecast has been calculated, these patient numbers need to be converted into quantities of drugs. The following steps should be completed to come up with a forecast quantity for each ARV drug required to treat those patients:

- Confirm the list of products that will be included in the forecast.

- Convert the forecasting data and assumptions into the total estimated quantity of each product to be dispensed for each year of the forecast.
- On the basis of current STGs, multiply the number of basic units of product (tablet, capsule, bottle, ml of liquid, etc.) that should be dispensed per patient, per day, and per year.
- Multiply by the total estimated number of patients expected to be treated each month or year.

Country Example: Calculate the need for d4T/3TC/NVP

- Because the total numbers of patients will be increasing each month, a monthly forecast must be calculated.
- For month 1, year 1, there will be 46,837 patients on the first line regimen of stavudine + lamivudine + nevirapine (this includes 2,646 new patients).
- Every patient will be on the triple fixed dose combination of d4T/3TC/NVP.
- Each patient will take 2 tablets of d4T/3TC/NVP every day.
- To calculate the total d4T/3TC/NVP needed for month 1, take the number of patients on this regimen (46,837) and multiply this by 2 tablets per day and multiply by 30 days per month.

$$46,837 \times 2 \times 30 = 2,810,220 \text{ tablets needed}$$

- Divide the total number of tablets into the pack size for the product. d4T/3TC/NVP comes in bottles of 60, so this would mean $2,810,220/60 = 46,837$ bottles are needed for month 1 of year 1 of the quantification.

$$2,810,220 / 60 = 46,837 \text{ bottles for month 1 year 1}$$

- New patients will also need a 14-day supply each of d4T/3TC, or 1 tablet of d4T/3TC per patient per day.
- To calculate the total d4T/3TC needed for month 1, take the number of new patients on this regimen (2,646) and multiply this by 1 tablet per day and multiply by 14 days.

$$2,646 \times 1 \times 14 = 37,044 \text{ tablets needed}$$

- Divide the total number of tablets into the pack size for the product. d4T/3TC comes in bottles of 60, so this would mean $37,044/60 = 618$ bottles are needed for month 1 of year 1 of the quantification.

$$37,044 / 60 = 618 \text{ bottles for month 1, year 1}$$

For programs that are scaling up or planning to implement significant changes in policies or strategies that will affect the demand for products, the forecasted quantity of each product to be dispensed should be estimated on a monthly basis for each year of the forecast. The same rule is applicable if there is a policy decision to introduce new products or replace the existing ones with others during the year for which there are no historical data.

CONSIDERATIONS FOR FORECASTING PEDIATRIC ARV DRUGS

Forecasting demand consumption of pediatric ARVs is even more complex than is forecasting demand for adult ART. The level of detail required to forecast the quantities of pediatric ARV drugs needed for a specific number of patients reflects the general complexity and sophistication required for diagnosis, care, and treatment of pediatric ART patients.

Although the basic method and approach do not differ, a number of key factors can influence and complicate the provision of pediatric ART services and the use of pediatric ARV drugs that must be addressed in the forecast. Those key factors include the following:

- Prescribing and dispensing of pediatric ARV drugs is complicated by the combined use of liquid, capsule, tablet, and FDC formulations.
- Formulations need to be changed and dosages need to be adjusted over time as the child grows.
- Adult ARV drug formulations can be used for children and may need to be cut or crushed to meet pediatric dosing requirements.
- Patient adherence is difficult because of the complicated dosing, the large volumes, and the palatability of liquid formulations, and young children's inability to swallow pills.
- Selection and availability of ARV drug formulations for children are limited, and the cost of pediatric formulations is high relative to adult formulations.
- Many pediatric ARV formulations are bulky liquids that require additional storage space and refrigeration.
- Pediatric ARV drugs are not packaged according to dosing schedules, which complicates prescribing and dispensing.
- Pediatric doses are often reconstituted at service delivery levels and must be discarded after a certain period. The volume of use within that period is unpredictable and can vary from site to site.

The following additional steps must be incorporated into the assumptions and calculations in order to estimate ARV drug requirements for children on ART:

Step 1. Calculate the number of pediatric patients who are expected to initiate ART during the forecast period. This number may be based on the number of children estimated to be on ART as a proportion of the total number of patients on ART for the forecast year. If data are available, the number may be based on an expected increase in the number of pediatric patients at ART sites in accordance with program expansion plans and historical uptake of pediatric patients.

Country example: Number of patients that will initiate ART

The total number of children on ART at the end of 2008 was 11,534. A total of 7,385 patients would be added during year 1 and 7,034 patients would be added during year 2.

Step 2. Apply a default rate to capture the number of pediatric patients who may discontinue treatment during the forecast period. Because experience in pediatric ART service provision is still relatively limited, this default rate is heavily informed by assumptions.

Country example: Default rate

A default rate of 10% was applied.

Step 3. Apply a monthly scale-up rate to capture the gradual increase in the number of pediatric patients on ART over the forecast period.

Country example: Phasing-in rate

New patients would be added uniformly during each month. For year 1, 615 (or 7385/12), patients per month would be added. During year 2, 586 (7,034/12) patients would be added.

Step 4. Verify the list of pediatric ART regimens being provided, and the percentage of patients on each regimen.

Country example: Pediatric regimens

The regimens were obtained from the STGs. Data on the percentage of children on ART by regimen were obtained from a thorough review of prescription data (from patient records and pharmacy dispensing registers) at the country's largest hospital. These are as follows:

First line regimens (99% of children)

- d4T/3TC/NVP: 40%
- d4T/3TC + EFV: 5%
- AZT/3TC + NVP: 40%
- AZT/3TC + EFV: 15%

Second line regimens (1% of children)

- ABC + ddl + LPV/r: 89%
- AZT + ddl + LPV/r: 11%

Step 5. Verify and document the pediatric dosages and formulations of each ARV drug.

Country example: Drugs

The following products were included:

- ABC 20 mg/ml solution
- ddl 25 mg tablets
- ddl 2 g/150 ml reconstitute 200 ml
- EFV 50 mg capsules
- 3TC 10 mg/ml solution
- d4T/3TC/NVP 6/30/50 mg tablets
- d4T/3TC/NVP 12/60/100 mg tablets
- LPV/r 80/20 mg/ml solution
- NVP 100 mg/ml solution
- d4T 15 mg capsules
- d4T 20 mg capsules
- d4T 1 mg/ml solution
- AZT 10 mg/ml solution
- AZT 100 mg capsules

Step 6. Categorize the pediatric patients on each ART regimen by age and by weight band:

Country example: Patients by weight band

Data on the percentage of children in each weight band were obtained from a thorough review of pediatric ART guidelines and prescription data (from patient records and pharmacy dispensing registers) at the country's largest hospital. The following weight bands were utilized:

- 3.0–4.9 kg
- 5.0–9.9 kg
- 10–14.9 kg
- 15–19.9 kg
- 20–24.9 kg
- 25–29.9 kg

The number of children was divided further by weight band within each regimen. For example, for patients on d4T/3TC/NVP, it was assumed that—

- 3.0–4.9 kg: 0%
- 5.0–9.9 kg: 10%
- 10–14.9 kg: 23%
- 15–19.9 kg: 28%
- 20–24.9 kg: 23%
- 25–29.9 kg: 14%

The age grouping, which typically stratifies children under 3 years of age and over 3 years of age, is designed to quantify liquid formulations for young children who are not yet able to swallow tablets or capsules, and to avoid the use of efavirenz, which is contraindicated for children under 3 years of age.

- Step 7.** Calculate the number of basic units (tablet, capsule, or milliliters of liquid) of each ARV drug required per day for each patient within each of the weight band groups. Liquid formulations must be calculated in milliliters (ml) at this point to determine the number of basic units required per patient per day.

In cases in which adult formulations are used to treat children, calculate the adjusted dosages of the adult ARV drug formulations that will be used for children (e.g., one-half tablet of AZT 300 mg/3TC 150 mg; use of EFV 50 mg capsules).

Country Example: Calculating drugs required

- Because the number of pediatric patients on ART will be increasing each month, a monthly forecast must be calculated.
- It is estimated that for month 1, year 1, there will be 4,568 patients on the first line regimen of AZT + 3TC + NVP (this includes 246 new patients that initiate therapy in month 1).
- Calculate the number of patients by weight band. For example, of the 4,568 patients on AZT + 3TC + NVP during month 1, year 1 of the quantification, it was estimated that 23% of these patients would weigh between 10 and 14.9 kg. This is a total of 1,050 patients.
- Determine the dose per kg for each product in the regimen. According to the guidelines, this is 60 mg/kg of NVP, 50 mg/kg of 3TC, and 130 mg/kg of AZT.
- Convert the dosing in mg to number of ml. To do this, the concentration of each of the drugs must be used. All three products in this regimen are produced as 10 mg/1 ml. This equates to 6 ml of NVP, 5 ml of 3TC, and 13 ml of AZT.
- Calculate the monthly need for each product as in the following example:

NVP: 1,050 patients x 6 ml x 2 times per day x 30 days = 378,000 ml

3TC: 1,050 patients x 5 ml x 2 times per day x 30 days = 315,000 ml

AZT: 1,050 patients x 13 ml x 2 times per day x 30 days = 819,000 ml

- Divide the total number of mls into the pack size for the product. NVP 10 mg/ml is packaged as 240 ml bottle.

$378,000/240 = 1,575$ bottles needed for month 1, year 1

(This is the quantity of NVP syrup required only for patients on AZT + 3TC + NVP for patients weighing between 10 and 14.9 kg. This calculation must be done for each weight band.)

Step 8. Multiply the basic number of units of each ARV drug product required per day by the total number of patient-days for each forecast year.

Country example: Calculating needs for a year

Because the numbers of patients will be increasing each month, monthly forecast consumption should be calculated. Each one of the monthly forecast figures should be added together to determine the total needs for the year.

Step 9. Add the total quantity required of each ARV drug product within all regimens and across all groups organized by age and weight band for each forecast year.

Country example: Calculating needs for a year

The total quantities needed have been calculated by regimen. When one product with the same formulation is used in more than one regimen, the quantities in these different regimens must be added together. For example, AZT solution is used in the following regimens:

- AZT + 3TC + NVP
- AZT + 3TC + EFV
- AZT + ddl + LPV/r

All of the uses of AZT solution should be added together to determine the total quantities of AZT solution required.

SUMMARY OF CHALLENGES AND LESSONS LEARNED IN QUANTIFICATION OF ARV DRUGS

COMMON CHALLENGES

While preparing national-level ARV drug quantification in the different countries, the USAID | DELIVER PROJECT identified a number of common and consistent challenges. The following challenges were the key guiding principles in developing the approach to forecasting presented in this companion.

- Although increasing numbers of programs are investing in developing and strengthening the LMIS, in general data on ART services and ARV drug supply are still of limited quality and availability and tend to be unreliable or insufficient for forecasting ARV drug requirements. Consequently, many forecasts still rely heavily on assumptions.
- STGs may be inconsistent, often need revision, and may not have been widely disseminated to providers. If disseminated, their consistent use may not have been reinforced, with the result that using STGs as assumptions during a forecast may have mixed results.
- Program targets may not take into account the service delivery capacity to increase enrollment of new patients and to continue monitoring existing patients on ART; the supply chain capacity to procure, deliver, and manage greater volumes of ARV drugs; or the program's capacity to finance sustained enrollment of new patients and maintenance of existing patients on ART.
- Program expansion rarely proceeds at the rapid pace that programs expect.
- Multiple sources of funding, procurement mechanisms, and distribution channels are used for ARV drugs, and aligning the funding, supply, and distribution streams to maximize product availability and supply chain performance is limited by insufficient mechanisms for and commitment to coordination and communication.
- Worldwide shortages of raw materials for the manufacture of ARV drugs and other limitations in supplier production capacity may need to be addressed in the quantification to identify alternate sources of supply for the required quantities of a product.

LESSONS LEARNED

As with the challenges, the following lessons learned have been incorporated into the approach to forecasting ARV drugs presented in this companion. The lessons are especially pertinent given that many ART programs still experience unpredictable demand.

- In the absence of reliable data, developing assumptions that are strongly informed by service providers and program managers is likely to enhance the reliability of forecast results.
- Preparing frequent updates of the quantification in general, but especially of the forecast, builds in the flexibility and agility necessary to ensure that if assumptions do not hold true, shipment quantities or timing can be adjusted to accommodate changing needs.
- Conducting advocacy for interventions that are outside of the quantification activity but that nonetheless impact successful quantifications—such as developing and maintaining a robust LMIS and developing a commodity security strategy to ensure long-term financing for ARV drugs—is critical to ensuring that the overall supply chain can be strengthened and that quantification can become increasingly effective and institutionalized over time.

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