Costing of HIV/AIDS Treatment in Mexico

March 2003

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- *To participate in the development and implementation of INSP's academic courses and extramural programs.*
- *To offer technical assistance to health service providers and institutions of higher education in the areas of research, training, and development of human resources, organizational structures and health service delivery.*
- *To participate in the design and implementation of community and health services intervention projects oriented toward the improvement of local health conditions.*

Abstract

This study documents the Mexican experience in HIV/AIDS treatment in three different health subsystems—the Ministry of Health, Mexican Social Security Institutes, and the National Institutes of Health. Ultimately, the study will provide donors and policy makers the information necessary to guide planning and scaling up of comprehensive HIV/AIDS treatment. The study consisted of a multicenter, retrospective patient chart review and the collection of complementary cost data to describe the utilization of services and to estimate costs of care for adult (18 years of age and above) HIV+ patients in the public sector who had at least one visit to a health facility between January 1, 2000, and December 31, 2001.

Researchers found that since antiretroviral drugs are the greatest single component within treatment cost, even a small reduction in drug costs would have a measurable impact on the overall cost of therapy. Other findings highlight several improvements that can be made in the quality of care patients are receiving.

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Acronyms

3TC	Lamivudine
AIDS	Acquired Immuno-Deficiency Syndrome
ARVs	Antiretroviral Drugs
AZT	Zidovudine
CD4	Cell Differential T Lymphocyte Count
CDC	Centers for Disease Control
CENSIDA	Mexican National Center for the Prevention and Control of AIDS
COESIDA	Mexican State Council for Prevention and Control of AIDS
CONASIDA	Mexican National Council for Prevention and Control of AIDS
d4T	Stavudine
ddC	Zalcitabine
ddI	Didanosine
ED	Emergency Department
ELISA	Enzyme-Linked Immunosorbent Assay
FONSIDA	Mexican National Fund for Persons Living with HIV/AIDS
GDP	Gross Domestic Product
GNP	Gross National Product
HAART	Highly Active Anti-Retroviral Therapy
HIV	Human Immuno-Deficiency Virus
ICU	Intensive Care Unit
INEGI	*Instituto Nacional de Estadistica Geografica e Informatica*
IMSS	Mexican Social Security Institute
INS	Mexican National Institutes of Health
INSP	*Insituto Nacional de Salud Publica* (Mexican National Institute of Public Health)
ISSSTE	Mexican Social Security and Services Institute for Workers of the State
LMIC	Low- and Middle-Income Countries
NGO	Nongovernmental Organization
OI	Opportunistic Infections

PAHO	Pan American Health Organization
PCP	Pneumocystis carinii pneumonia
PHR*plus*	Partners for Health Reform*plus* Project (USAID)
PLHA	People Living with HIV/AIDS
SSA	Mexican Ministry of Health
STI	Sexually Transmitted Infection
UNGASS	United Nations General Assembly Special Session on HIV/AIDS
UNAM	University of Mexico
USAID	United States Agency for International Development
WHO	World Health Organization

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Executive Summary

Mexico ranks 13th globally and third in the Americas in the total number of HIV cases reported. While AIDS is the 16th leading cause of death in Mexico, it jumps to as high as fourth when only men aged 25 to 34 are considered (Uribe Zuñiga 1998). The disease has been reported in all 32 states of Mexico. According to official reports, as of December 2001, a total of 51,914 cumulative cases of AIDS had been recorded in Mexico (CONASIDA 2002a). Delays and underestimation in reporting, however, raise that number to a government estimate of as many as 64,000 cases, with an additional 116,000 to 177,000 people currently infected with HIV (CONASIDA 2002b).

Antiretroviral drugs (ARVs), especially when used in combinations of three or more, have dramatically improved the health and lives of people living with HIV/AIDS (PLHA) around the world (Wood et al. 2000, Wilkinson et al. 1998). However, the high cost and substantial clinical requirements of providing these drugs have, until recently, put them out of reach of the vast majority of PLHA in low- and middle-income countries (LMICs). This situation has recently changed, reflecting the confluence of two factors: First, the costs of ARV therapy in Latin American and Caribbean countries dropped as much as 54 percent from 2001 to 2002 as a result of negotiations between ministries of health and pharmaceutical companies, with some figures for triple combination ARVs quoted at less than 1/12 of 2001 retail prices (Pan American Health Organization/World Health Organization 2002)[1]. This price reduction has a substantial impact on the affordability of therapy. Second, the United Nations has intensified its efforts to combat AIDS.

Access to treatment, including ARVs, and care for PLHA in Mexico varies considerably across socioeconomic groups (Saavedra 1998). Since 1992, Mexico's five social security institutions have offered access to free HIV/AIDS care from specialists at secondary and tertiary hospitals. However, the uninsured that seek care at Ministry of Health facilities have had a much more difficult time receiving ARV treatment. ARVs remain out of reach for the poor and those who do not have access to social insurance or to the state's FONSIDA (Mexican National Fund for Persons Living with HIV/AIDS) program. To address this gap, the Minister of Health has committed to providing, by 2006, ARV treatment to everyone who needs it.

There is a growing body of literature on the costs of providing ARV treatment in industrialized nations. Extensive cost and cost-effectiveness studies on ARV treatment have been conducted, largely in these countries (Schrappe and Lauterbach1998). For example, data collected in the United States reveal the progression of ARV treatment options, from monotherapy (Hellinger and Fleishman1993, Bozette et al.1994) to Highly Active Anti-Retroviral Therapy (HAART) (Freedberg et al. 2001, Hellinger and Fleishman 2000, 1999, Schrappe and Lauterbach 1998). Both macro- and micro-level cost data have been collected from various sources: national surveys (Bozette et al. 2001); costs of particular hospital, state, or government programs (Mauskopf et al. 2000); and costs to employers for HIV-infected workers (Farnham and Gorsky 1994). Similar studies have been conducted in Europe, where national use and costs of hospital care by stage of HIV infection (Beck et al. 1998), costs of

[1] Generic production and/or purchasing from unlicensed producers (e.g., Brazil, South Africa) also contributed to the reduction in drug prices.

particular hospital programs (Dijkgraaf et al. 1995), lifetime treatment costs per patient (Jebakumar et al. 1995), annual drug costs (Anis et al. 1998), and cost-effectiveness of universal access to HAART (Sendi et al. 1999) have been considered.

The purpose of this study was to document the Mexican experience in HIV/AIDS treatment in three different health subsystems—the Ministry of Health (SSA), Mexican Social Security Institutes (IMSS/ISSSTE), and the National Institutes of Health (INS)—using a consistent methodology to provide donors and policy makers the information necessary to guide planning and scaling up of comprehensive HIV/AIDS treatment. Specifically, the information will allow policy makers to compare the relative costs of specific treatment categories and to estimate the total costs of ARV treatment programs, including non-drug costs.

Researchers conducted a multicenter, retrospective patient chart review and collected complementary cost data to describe the utilization of services and estimate costs of care for adult (18 years of age and above) HIV+ patients in the public sector in Mexico. These patients had to have made at least one visit to a Mexican health subsystem between January 1, 2000, and December 31, 2001. Comprehensive data on patient sociodemographic characteristics; clinical events; use of outpatient, inpatient, and laboratory services; and use of medications was captured from medical charts of 1062 HIV+ patients registered in one of 11 study sites using a structured computer-based interface. The interface was programmed in Microsoft Visual Basic 6 and the data stored in Microsoft Access 2000. Data on costing practices and the cost components of ambulatory, inpatient, and laboratory services and medications were gathered using a structured computer-based interface programmed in Microsoft Excel XP 2002.

A total of 11 health facilities were selected for the study. Sites were chosen to reflect several criteria, including health subsystem, geographic location, and level of care. To ensure representation of the three health subsystems providing care for PLHA in the public sector in Mexico, five sites were selected from the SSA, four from the IMSS/ISSTE, and two from the INS. As costs and patterns of care are likely to differ considerably between Mexico's largest urban center, Mexico City, and other areas of the country, researchers selected facilities from three major urban centers: Mexico City (six), Guadalajara (three) and Cuernavaca (two). These centers are located in the states with the highest number of accumulated AIDS rates (CONASIDA 2002). Since both the HIV cases and HIV patient care are concentrated in urban areas, the cities selected captured most of the HIV patients receiving care in these states.

The sample population is primarily male (70.4 to 83.5 percent), as is the case with the general PLHA in Mexico (84 percent). Similarly, the principal mode of transmission is sexual (94.3 to 95.8 percent in the study sample; 89.8 percent in the PLHA), and the epidemic is concentrated among men who have sex with men (59.1 percent in the INS, 59.6 percent in the SSA, and 61 percent in the PLHA). IMSS is an exception with 61.7 percent of respondents identified as heterosexual—a statistically significant difference. Authors speculate that there may be bias in reporting sexual preference due to stigma or fear of discrimination since social security coverage is employment based. This line of inquiry was not pursued since it is outside the purview of this study.

Despite serious efforts made to include a wide range of different types of institutions providing care to PLHA in this study sample and the fact that the characteristics of the PLHA in the sample are not dramatically different from those reported by the National AIDS Program, one should be very cautious in extrapolating these results to the entire country. The sample is *neither* nationally representative *nor* weighted to reflect the proportions nationally of PLHA not eligible for HAART, eligible but not receiving HAART, and receiving HAART.

The education level of the IMSS/ISSSTE sample population differs significantly from the sample averages for the other subsystems, which are similar to the national average. Relative to the national average, a much lower percentage of IMSS/ISSSTE patients, 9 percent compared with 28.2 percent nationally, completed primary education or less, while a much higher percentage, 38.2 percent compared with 12.1 percent nationally, reached the university level. This is not unique to the PLHA seeking care in social security facilities. It probably reflects schooling characteristics of the insured population, which is by the nature of its formal sector employment more likely to be educated.

Several findings and conclusions can be drawn from this study, although it must be stressed that these conclusions refer to the study sample. First, there has been a progressive and rapid move towards triple therapy. In 1997, 69.4 percent of patients receiving ARVs were on double therapy and only 26.4 percent were on triple therapy. By 2001 the vast majority of patients (88.1 percent) were on a three-drug regiment while the share of double therapy recipients had dropped to 10.1 percent. The number of patients on monotherapy has also decreased steadily, although a small number of patients remain on a single medication despite treatment guidelines that recommend triple therapy as the norm and double therapy in exceptional cases

Second, data from the study confirm the commonly held belief that initiation of triple therapy treatment in Mexico occurs only once patients are very ill. Despite norms that state that double therapy should only be used when the CD4 count exceeds 350 cells/mm^3, in the year leading up to initiation of triple therapy the median CD4 count was well below that, at 150 cells/mm^3. Further, in Year 1 there is a high concentration of patients around the median, indicating that a large number of patients who likely qualify for triple therapy are receiving either double, mono, or no ARV therapy.

Third, there is a substantial benefit to ARV therapy, as indicated by the surrogate marker CD4. Although improvement in CD4 counts is gradual, with the median rising to 292 cells/mm^3 in Year 3 from 180 cells/mm^3 in Year 1, the rate of improvement is in line with what would be expected since patients on triple therapy generally have an average CD4 increase of 75-100/mm^3 per year. Three years after initiation of triple therapy there is wider variance in CD4 levels across patients, with some patients responding well while others do not.

Fourth, there is a marked increase in the average annual cost per patient after initiation of triple therapy. This is primarily due to the cost of ARVs. These drugs are the single largest cost component throughout the study period, but their contribution to total cost jumps significantly once patients are started on triple therapy. Pre-HAART, ARVs account for 35.2 to 59.4 percent of total costs, whereas their share increases to 72.7 to 78.3 percent of total costs post-HAART.

Fifth, the study clearly reveals that ARVs are not cost saving. Once patients begin taking ARVs, total utilization increases. Although results show a decline in hospital days after patients begin triple therapy, this decline is not nearly large enough to offset the increase in costs attributable to ARVs. This is inconsistent with data from a Brazilian study which showed that ARVs actually have a cost-saving effect due to the sharp decline in annual AIDS-related admissions per patient following the introduction of HAART (Ministry of Health (Brazil), 2003). Furthermore, the effect of these drugs is to prolong life, postponing the burden of hospitalization costs.

Finally, study findings indicate that no institution completely follows the normal procedures for treatment, despite the fact that these norms are “official” and supposedly obligatory. Inconsistent patterns of treatment suggest important room for quality improvement, independent of purchase of drugs. In many cases, the treating doctor prescribes a regimen that reflects his or her personal beliefs about what is best for the patient, rather than a regimen that follows the official norms. Furthermore,

the official norms are not updated regularly enough to reflect the most recent advances in technology and knowledge. The current norms for example were developed in 2000, and although, as mentioned above, a new version has been formulated, this new version has not yet been made official.

Several conclusions and policy recommendations can be drawn from this study. At the facility level, there needs to be a greater level of standardization in terms of the quality of care offered, since it appears that treatment in the mainstream does not conform to the official norms and guidelines. Some investigation of why this is the case is perhaps necessary; it could possibly be because physicians do not have at their disposal sufficient resources to provide the level of care set out in CENSIDA's (Mexican National Center for the Prevention and Control of AIDS) guidelines. It could also be due to insufficient physician training and inexperience in the treatment of HIV. There may, therefore, be a scope for additional training for physicians who are already treating HIV patients, as well as for investigating the importance placed on HIV/AIDS in university curriculums for physicians and specialists in infectious diseases. This aspect warrants further study.

ARVs constitute the largest proportion of costs for HIV patients, and should, in fact, be larger if one takes into account that the study data most likely underestimate ARV utilization. The Mexican government, like all governments in developing countries facing large costs for the treatment of HIV/AIDS, is very concerned about the cost of ARVs and is exploring a number of responses. It has already undertaken multiple rounds of negotiations with pharmaceutical manufacturers and has achieved important reductions in the cost of many ARVs. However, Mexico has achieved far less success in this area than countries such as Brazil, India, Thailand, and South Africa that have either developed a domestic ARV drug production capacity or openly considered the possibility.

Introduction

Antiretroviral drugs (ARVs), especially when used in combinations of three or more, have dramatically improved the health and lives of people living with HIV/AIDS (PLHA) around the world (Wood et al. 2000, Wilkinson et al. 1998). However, the high cost and substantial clinical requirements of providing these drugs have, until recently, put them out of reach of the vast majority of PLHA in low- and middle-income countries (LMICs). This situation has recently changed, reflecting the confluence of two factors: First, the costs of ARV therapy in Latin American and Caribbean countries dropped up to 54 percent from 2001 to 2002 as a result of negotiations between ministries of health and pharmaceutical companies, with some figures for triple combination ARVs quoted at less than 1/12 of 2001 retail prices (Pan American Health Organization/World Health Organization, 2002). This price reduction has a substantial impact on the affordability of therapy. Second, the United Nations has intensified its efforts to combat AIDS. The June 2001 Declaration of Commitment on HIV/AIDS set ambitious goals for reducing incidence through a dual strategy of expanding prevention efforts and increasing access to care and support for all PLHA (UNGASS, 2001). Consequently, several ministries of health and governments in LMICs have committed to providing treatment to all who need it.

There is a growing body of literature on the costs of providing ARV treatment in industrialized nations. Extensive cost and cost-effectiveness studies on ARV treatment have already been conducted, largely in these countries (Schrappe 1998). For example, data collected in the United States reveal the progression of ARV treatment options, from monotherapy (Hellinger 1993, Bozette et al. 1994) to Highly Active Anti-Retroviral Therapy (HAART) (Freedberg et al. 2001, Hellinger and Fleishman 2000, Gebo 1999, Schrappe and Lauterbach1998). Both macro- and micro-level cost data have been collected from various sources: national surveys (Bozette et al. 2001); costs of particular hospital, state, or government programs (Mauskopf et al. 2000); and costs to employers for HIV-infected workers (Farnham and Gorsky 1994). Similar studies have been conducted in Europe, where national use and costs of hospital care by stage of HIV infection (Beck et al. 1998), costs of particular hospital programs (Dijkgraaf et al. 1995), lifetime treatment costs per patient (Jebakumar et al. 1995), annual drug costs (Anis 1998), and cost-effectiveness of universal access to HAART (Sendi et al. 1999) have been considered.

As with any study of this nature, there are some limitations that need to be clearly spelled out. An important characteristic of this kind of (retrospective) study is that there is no guarantee that patient records contain all the necessary and relevant information; therefore, data may underestimate actual utilization. This seems to be true particularly in the case of ARVs and prophylactic medicine for opportunistic infections, i.e. drugs that are prescribed on a repetitive basis. In addition, information on the number of days of treatment and dosage were very often not included in the patient records, and these therefore had to be imputed, given standard practice and patient diagnosis.

The sample was not designed to be representative at the national level, but rather to reflect the situation in major treatment centers; therefore, although three very important locations were chosen for this study in terms of the number of accumulated cases of HIV/AIDS, the costs and methods of treatment may differ in other Mexican states. Additionally, the sample of patients within each hospital was not chosen randomly; rather, researchers chose a proportion of patients on ARVs, patients who

were not taking ARV therapy, and deceased patients, so as to be able to collect meaningful data from each of these three groups. Within each of these groups, a random sample of patients met the inclusion criteria.

1. Purpose

The purpose of this study was to document the Mexican experience in HIV/AIDS treatment in three different health subsystems—the Ministry of Health (SSA), Mexican Social Security Institutes (IMSS/ISSSTE), and the National Institutes of Health (INS)—focusing on the changes in utilization of services and cost patterns associated with the introduction of Highly Active Anti-Retroviral Therapy (HAART). The study uses a consistent methodology to provide donors and policy makers the information necessary to guide planning and scaling up of comprehensive HIV/AIDS treatment. Specifically, the information will allow policy makers to compare the relative costs of specific treatment categories and to estimate the total costs of antiretroviral (ARV) treatment programs, including non-drug costs. The specific objectives of this study were the following:

- Identify patterns of care and treatment costs for patients from the following treatment categories:
  - Routine ambulatory care for patients receiving ARV therapy
  - Routine ambulatory care for patients not receiving ARV therapy
- Estimate annual care costs per patient, qualified by the following:
  - Disease stage (CD4, viral load)
  - Health subsystem (SSA, IMSS/ISSSTE, INS)
  - Care setting (outpatient, inpatient)
  - Level of care (specialized care clinics, secondary hospitals, tertiary hospitals)
  - Geographical location (Mexico City, Morelos, Jalisco)
  - Type of therapy received (ARV triple therapy or not)

2. Background

2.1 Socioeconomic Situation

Mexico is an upper middle-income country with a per capita Gross Domestic Product (GDP) of US $5,070 in 2001, ranking 68th globally and third in Latin America. It is the third most populous country in the Americas, with a population of over 99.5 million people[2] (World Bank 2002). Roughly 75 percent of the population is concentrated in urban areas (INEGI 2002). In 2001, total spending on health equaled 5.7 percent of GDP, with approximately 48 percent of funds flowing though the public sector and 52 percent through the private sector (Secretaría de Salud, Mexico 2002).

Mexico's population is served by several coexisting public and private health care systems, to which access varies by socioeconomic standing and employment status. A very small, privileged group affords private insurance, while those from the middle of the spectrum generally use one of several parallel social insurance programs that are also direct providers of care. The social security system consists of five institutions, with the two largest being the IMSS for nongovernment workers employed in the formal sector and the Social Security and Services Institute for Workers of the State (ISSSTE) for government employees. The SSA serves mostly the poor uninsured, known as the "open population," as well as the employees of the informal sector of the economy. In 2000, about 40 percent of the population was estimated to be uninsured, and 60 percent was covered by one of the social security institutions, with the IMSS alone covering 47 percent of the general population (INEGI 2000). It is important to note that nearly 48 percent of health expenditures in Mexico are financed by out-of-pocket payments used primarily to purchase services from private providers, underscoring the high degree of fragmentation in revenue collection, pooling, and purchasing in the health system (World Health Organization 2000).

The Mexican health system is also characterized by geographical differences in access to care. For example, the uninsured living in Mexico City receive highly specialized care from the INS while some rural populations have limited access to basic care.

2.2 Health Sector Response to the HIV/AIDS Epidemic

Mexico ranks 13th globally and third in the Americas in the total number of HIV cases reported. While AIDS is the 16th leading cause of death in Mexico, it jumps to as high as fourth when only men aged 25 to 34 are considered (Uribe Zuñiga 1998). The disease has been reported in all 32 states of Mexico. According to official reports, as of December 2001, a total of 51,914 cumulative cases of AIDS had been recorded in Mexico (CONASIDA, 2002a). Delays and underestimation in reporting, however, raise that number to a government estimate of as many as 64,000 cases, with an additional 116,000 to 177,000 people currently infected with HIV (CONASIDA 2002).

[2] The estimate of population size refers to the *de facto* resident population, and not the *de jure* population.

The epidemic remains largely urban (96 percent of cases) (Magis et al. 1995) and male (91 percent) (CONASIDA/Secretaría de Salud 1998). The majority of accumulated cases (55 percent) are concentrated in the Federal District, the State of Mexico, and Jalisco (Uribe Zuñiga 1998). In Mexico, the main mode of transmission of HIV/AIDS is sexual (an estimated 86.7 percent of accumulated AIDS cases) and concentrated among men who have sex with men (between 28 and 40 percent of all cases of HIV infection) (CONASIDA 2002). Men represent 85.7 percent of accumulated AIDS cases, and the remaining 14.3 percent are women who become infected primarily through heterosexual transmission. Perinatal transmission accounts for 2 percent of the cumulative number of cases in Mexico (CONASIDA 2002). Transmission through blood transfusions is rare and has declined steadily since the onset of the epidemic.

In response to the AIDS epidemic, Mexico created the National Council for Prevention and Control of AIDS (CONASIDA) in 1988. CONASIDA was the official government agency charged with meeting the diverse challenges of the HIV/AIDS epidemic in Mexico. In line with decentralization, state versions of CONASIDA (called COESIDAs) were developed in some of Mexico's 32 states and each state has its own HIV/AIDS program (CONASIDA 2001). In 2001, the council's name was changed to the National Center for the Prevention and Control of AIDS (CENSIDA). Although initial financial support came from international donors, by 1998 more than 90 percent of funds for CENSIDA came from the Mexican government.

CENSIDA's activities are primarily focused on the prevention of HIV transmission; reduction of the impact of HIV on individuals, families, and society; and coordination of institutional, interinstitutional, territorial, and intersectorial programs. CENSIDA also closely coordinates with Mexico's 138 nongovernmental organizations (NGOs) and organizations of persons who live with HIV/AIDS.

2.3 Study Perspective

This study examines the cost of care from the perspective of the managers of publicly funded health services in Mexico. Thus, it considers only those costs paid directly by the public sector and not those borne by patients, whether those costs are to access services in the public sector or to receive parallel care from the private sector. While it would be desirable to extend the study to consider a social perspective, the purely retrospective, record-based nature of the study precluded consideration of costs that were not borne by the health system. The Mexican National Institute of Public Health, in collaboration with several of the clinical centers studied here and the National AIDS Program, is seeking funding to extend the present work to enable prospective data collection and thus reexamine costs of care from a social perspective.

3. Antiretroviral Treatment

Access to treatment, including ARVs, and care for people living with HIV/AIDS (PLHA) varies considerably across socioeconomic groups (Saavedra 1998). Since 1992, Mexico's five social security institutions have offered access to free HIV/AIDS care from specialists in tertiary hospitals and/or secondary hospitals that have specialists on staff. However, the uninsured that seek care at Ministry of Health facilities have had a much more difficult time receiving ARV treatment. ARVs remain out of reach for the poor and those who do not have access to social insurance or to the state's FONSIDA (Mexican National Fund for Persons Living with HIV/AIDS) program. To address this gap, the Minister of Health has committed to providing, by 2006, ARV treatment to everyone who needs it.

ARV treatment in the private sector also varies considerably. NGOs have been providing treatment for uninsured PLHA in 25 Mexican states (Saavedra et al. 1998). Although their reach in terms of the number of people receiving ARVs is limited, NGOs play an important role. [3] For instance, in some cases, ARVs were available through NGOs before they became available through the formal pharmaceutical sector, possibly speeding the process of inclusion of ARVs into the Essential Drug List. Private insurance does not usually cover ARVs. In Mexico, most of the spending on treatment for patients without social security comes from the patient's own pocket, sometimes with the support of family, friends, or private donors (Saavedra et al. 1998). Mexico, like many middle-income countries, started using ARVs in the late 1990s. In 1997, only Zidovudine (AZT), Indinavir, Ritonavir, and Saquinavir were listed on the Essential Drug List. By 2001, the following ARVs had been added to the list: Lamivudine/Zidovudine (COMBIVIR), Didanosine (ddI), Zalcitabine (ddC), Lamivudine (3TC), Stavudine (d4T), Nevirapine, and Efavirenz. All drugs on the Essential Drug List (including ARVs) are, absent stock-outs, provided free of charge to the populations with social security coverage.

3.1 The FONSIDA Program

In 1996, CONASIDA, despite its charge as a coordinating agency, began providing ARVs free of charge to a small part of the uninsured population. CONASIDA arranged with pharmaceutical companies for the free provision of ARVs to those enrolled in clinical trials. By 1997, the Mexican government asked CONASIDA to resume its role as a national coordinating agency and to stop providing ARVs. The government then created FONSIDA whose main purpose was to raise funds to purchase ARVs for the uninsured population. The SSA allocated initial funds; the University of Mexico (UNAM) provided free facilities, equipment, and personnel; and the Merck Foundation provided training for health personnel in charge of specialized services at the state level. The program's budget for 2002 was 150 million (in Mexican pesos), which allows for the continuation of treatment for existing patients as well as access to treatment for 1,900 new patients (CENSIDA web

[3] Izazola et al. estimate that 14 percent of AIDS patients receive care from NGOs. Only a subset of AIDS patients receives ARV treatment.

page). Individual states can make contributions to supplement FONSIDA's budget. As stated earlier, the aim is to have 100 percent of patients in need of ARVs covered by 2006.

To be eligible for the FONSIDA program, a patient must meet a number of criteria. First, a social worker must determine whether the patient has social security coverage (in which case he or she is disqualified) and whether he or she has limited socioeconomic means. Second, priority for treatment is usually given to children, pregnant women, and adult patients with low CD4 count (<300 cells/mm^3), high viral loads (>30,000 copies), and symptoms of advanced disease progression. There is a long waiting list for treatment, and many patients continue to pay for ARVs out of pocket or receive drugs through other channels, such as NGOs.

Apart from the FONSIDA program, approximately 300 patients receive ARVs from state funds, notably in Oaxaca, Michoacán, Aguascalientes, Sonora, and Yucatán. The aim is to decentralize the purchase of these drugs to the state level, since at the moment all new entrants to FONSIDA have to be approved by CENSIDA, a process that can take several months.

3.2 Official Mexican Norms for the Prevention and Control of HIV/AIDS

In 1995, the Mexican government developed a set of official norms for the prevention and control of HIV, including protocols for treatment. These protocols are supposedly obligatory, i.e., all patients, in theory, have the right to receive treatment of the level stated in the norms at any medical facility in the country, be it private or public (Norma Oficial Mexicana, Nom-010-SSA2-1993). The Ministry of Health and the governments of the individual states have the duty to ensure that these norms be respected. Notwithstanding, these norms have no legal standing.

According to the official norms, all clinicians treating persons with HIV should follow the recommendations set out in CENSIDA's Guide for Treatment of Patients with HIV/AIDS (CONASIDA 2000). These recommendations are summarized below.

Indications to initiate ARV treatment depend on the clinical state of the patient. The treatment of an adult patient should be based on disease stage and laboratory test results, in particular CD4 and total lymphocyte counts, as well as the determination of viral load. These tests should be performed at least once every six months. It is recommended that treatment be initiated in

(i) patients with symptomatic primary infection,

(ii) symptomatic patients, and

(iii) asymptomatic individuals with CD4 lymphocyte count <500/ mm^3 or with viral load of 10,000 copies/ml by bDNA or of 20,000 by RT PCR. In order to limit the development of resistance, the norms recommend the following:

- Treatment be initiated in early stages of the disease, with an aggressive scheme (at least double therapy) to achieve suppression of the viral load to undetectable levels
- Monotherapy not be utilized
- Double therapy be used only when CD4 >350 cells/mm^3or viral load is less than 20,000 copies/ml
- Adherence to the specified treatment be encouraged, avoiding both reduction of dosage or missed doses

- Risk of cross-resistance is considered when changing from one treatment scheme to another.

Additionally, prophylactic medication for tuberculosis should be given to patients with CD4 count of less than 500 cells/mm^3. When CD4 falls below 200 cells/mm^3, prophylaxis against PCP should be added to the regimen, as well as Itraconazol or Fluconazol to prevent fungal infections.

This treatment guide for 2000 is about to be updated. CENSIDA's new guidelines, which are in the process of being officially approved, recommend a later start for ARVs (CENSIDA 2002). According to this document, the following factors need to be considered before initiating therapy:

- The desire and commitment of the individual to begin ARV treatment
- A patient's level of immunodeficiency, determined by CD4 count
- Risk of disease progression, determined by levels of RNA of HIV in the plasma
- Potential benefits and risks of long-term use of the drugs.

For asymptomatic patients with CD4 counts greater than 350/mm^3, initiating ARV therapy is not currently recommended given that the risk of developing opportunistic infections is relatively low. But if the patient has a CD4 count below 200/mm^3, initiation of therapy is recommended independent of the patient's viral load and whether or not he/she is asymptomatic, since the risk of developing an opportunistic infection is significant.

When the CD4 count is between 200 and 350, the patient's level of viral load in the plasma is important in deciding whether to begin therapy or not. If viral load is greater than or equal to 55,000 copies/ml, the risk of progression is significant and, therefore, initiation of therapy is recommended. In those cases where viral load is below 55,000 copies, the risk of progression is much less and therapy can be postponed. However, it is also necessary to take into account the particular conditions of the patient and his or her choice. If the patient decides not to begin therapy, his or her CD4 count should be monitored closely (i.e., every 3 to 4 months).

With regard to patients who already show clinical manifestations of HIV, due to an opportunistic infection or neoplasia, treatment should start immediately.

4. Care of HIV/AIDS Patients Across Health Subsystems

High standards of care for HIV/AIDS patients are laid out in the official norms adopted by the Mexican government; however, financial, human resource, and infrastructure constraints hinder the delivery of optimal care. According to the National Action Program on HIV/AIDS and Sexually Transmitted Infections (STIs), in spite of the government's efforts, "… it has not yet been possible to offer high quality care, nor to cover all of the affected population." (CENSIDA 2001)

4.1 Secretaría

Geographic location. As mentioned earlier, most of the patients who receive care at SSA facilities receive ARVs through government funding, though a significant number are assisted by NGOs. Notwithstanding the recent increases in ARV coverage, an important share of PLHA does not have access to ARV treatment at all. This coverage pattern is highly variable from state to state and between urban and rural areas. For instance, the proportion of patients that have access to ARVs financed through FONSIDA in México City far exceeds the proportion in Guadalajara; this is because the resources available per PLHA in Mexico City are much greater than those available in Guadalajara.

Infrastructure capacity. Depending on the hospital's capacity, visits to the doctor for monitoring purposes are required once every one to three months. In more academic hospitals such as the Hospital Civil in Guadalajara and the National Institutes, where there are many medical interns and a higher level of physician specialisation and experience, patients are expected to visit their doctor for a monthly checkup. However, at secondary-level hospitals such as the Hospital General de Occidente, where staff capacity is overstretched, patients are given appointments on average once every three months, depending on their health status.

Lab capacity. Doctors recognize the ideal of performing two viral load and two CD4 count tests annually for HIV/AIDS patients, especially for those who are taking ARVs. In reality, however, one or two tests per year are the norm for CD4 counts. This depends on various factors: the capacity of the clinic or hospital to do the tests, whether or not there is a waiting list, and the patient's state of health. Also, more than one viral load test per patient per year is uncommon. Laboratories in public hospitals generally have the capacity to perform CD4 tests. Private laboratories, on the other hand, conduct viral load tests in many cases. Patients are usually entitled to a discount on the test, but the cost is still prohibitively high, at around 1400 pesos.

Drug availability. Hospitals generally dispense medications to prevent tuberculosis, such as Isoniazid, free of charge. However, patients may have to acquire other prophylactic medications, such as trimethoprim-sulfamethoxazole, from the pharmacy and pay out of pocket. There seems to be no clear policy on the dispensing of medicines. When medicines are available at the hospital, they are given free of charge. When they are not available, patients have to pay them out of pocket. This is the case with ARVs as well. A doctor at the HIV unit at the Hospital Civil (Guadalajara) estimates that up

to 30 percent of patients do not take prophylactic medication, either because of stock-outs or because the medicine is not offered free of charge and the patient cannot afford to pay for it.

4.2 IMSS

Lab capacity. Access to basic tests such as CD4 and viral load may also be lacking, as well as treatment by doctors who have experience with HIV patients (Saavedra 1998). Although patients do not have to pay for these tests, access may depend on other factors such as the availability of the tests in each hospital.

Human resource capacity. In general, the physicians responsible for treating HIV/AIDS cases are specialists in infections diseases. However, discussions with clinicians indicate that the medical personnel responsible for HIV/AIDS patients do not have sufficient clinical experience to deal with the disease, or personnel who have specific knowledge of HIV/AIDS may only be available on certain days, at certain times.

Drug availability. Based on anecdotal information from providers, the socially insured population, in theory, has access to ARVs; however, in practice this is not always the case. It is not uncommon for providers to be forced to modify, or even suspend, ARV treatment because of stock-outs. This can provoke patient resistance to the therapy.

4.3 INS

The situation at the INS differs from that in the IMSS/ISSSTE and SSA in that National Institute hospitals are tertiary level, with highly specialized physicians. The patients treated in these hospitals usually have good access to ARVs (through FONSIDA or through INS itself) and to good medical attention in general. Many of these patients participate in clinical studies, which guarantee them, at least for a certain period of time, a better level of treatment than those who are treated in the other two health subsystems.

As is the case in the SSA, private laboratories and INS hospitals often have agreements to provide laboratory tests at a discount for HIV/AIDS patients.

Many patients who are treated in the National Institutes also receive medical attention in other hospitals. This is in part because user fees are higher in the INS than in the SSA.

4.4 Future Goals

While the Mexican government recognizes that treatment for HIV/AIDS patients in the public sector is not ideal, it has made an explicit commitment to improve the situation.

The government's program has set out the following goals for action on HIV/AIDS and STI prevention and control for 2001-2006 (CENSIDA 2001):

- Reduce mortality from AIDS by 25 percent
- Broaden coverage of ARVs to all persons who require them

- Ensure that all HIV/AIDS patients have access to high-quality integrated care

The report proposes, among other things, that to achieve these goals, the quality of the services provided must be improved. This includes ensuring a consistent supply of medicines and inputs needed to treat HIV/AIDS. Another aim is to ensure the dissemination of and adherence to norms, guides, and guidelines for HIV care (although which norms should be followed is not stated), as well as to train health care providers in this area. To encourage greater adherence to treatment regimens, self-help groups are proposed. Also on the government's agenda is the lobbying of private insurers to urge them to provide coverage for HIV/AIDS.

For example, one of the most important projects in terms of access to treatment is a program called "Seguro Popular de Salud" (Public Health Insurance), which offers public health insurance for families and citizens who because of their employment or socioeconomic status are not insured with the social security institutions. Although the coverage offered is still not universal, at the moment it includes HIV testing and counseling, and it is hoped that, with time, the package of services will be expanded. The project has only recently been initiated, but it is one example of how the government is trying to improve access to care for the uninsured population.

Nevertheless, to be able to plan and carry out an increase in coverage and access to drugs and treatment in general for patients with HIV/AIDS, the government needs more reliable and detailed information regarding the costs and benefits of expanding the treatment program. In this regard, it is of vital importance to generate this information to allow the government to make better informed decisions.

5. Methodology

5.1 Study Design

Researchers conducted a multicenter, retrospective patient chart review and collected complementary cost data to describe the utilization of services and estimate costs of care for adult (18 years of age and above) HIV+ patients in the public sector in Mexico. Patients had to have made at least one visit to a Mexican health subsystem between January 1, 2000, and December 31, 2001.

5.2 Study Population

Information was captured from the medical charts of 1062 HIV+ patients registered in one of 11 study sites and through collection of complementary unit cost information from each site.

5.3 Site Selection

A total of 11 health facilities were selected for the study. Sites were chosen to reflect several criteria, including health subsystem, geographic location, and level of care. To ensure representation of the three health subsystems providing care for PLHA in the public sector in Mexico, five sites were selected from the SSA, four from the IMSS/ISSTE, and two from the INS. As costs and patterns of care are likely to differ considerably between Mexico's largest urban center, Mexico City, and other areas of the country, researchers selected facilities from three major urban centers: Mexico City (six), Guadalajara (three) and Cuernavaca (two), as shown in Table 1. These centers are located in the states with the highest number of accumulated AIDS rates (CONASIDA 2002). Since HIV cases and HIV patient care are both concentrated in urban areas, the cities selected should capture most of HIV patients receiving care in these states. Finally, researchers selected a variety of facility types, including highly specialized tertiary care hospitals (two), secondary care hospitals (eight), and specialized HIV outpatient clinics (one).

Table 1. Type of Facility by Health Subsystem and Geographic Location

City, state	Subsystem				TOTAL
	SSA	IMSS	ISSTE	INS	
Mexico City / Federal District	2	2	0	2	6
Guadalajara, Jalisco	2	0	1	0	3
Cuernavaca, Morelos	1	1	0	0	2
Total	5	3	1	2	11

5.4 Subject Eligibility

Patients meeting the following jointly applied criteria were eligible for inclusion in the study:

- Diagnosis of HIV infection confirmed by Enzyme-Linked Immunosorbent Assay (ELISA), Western Blot, or laboratory culture, or symptomatic AIDS
- 18 years of age or older at the time of first consultation
- At least one documented medical visit at a study site within the period January 1, 2000, to December 31, 2001. For those included in the study, data were captured retrospectively for a period of three years as calculated from the last consultation in the period January 1, 2000, to December 31, 2001, or until initiation of the HIV dossier.

5.5 Sampling Framework

A sample of patients was selected from each study site. The sampling framework was based on convenience, and aimed to reflect clinical and treatment criteria of interest. Researchers deliberately over-sampled those initiating ARV treatment in the study time period (to increase statistical power to detect costs and effects) and those who died during the study time period (to increase power to estimate lifetime costs, given the concentration of costs at the end of life). Specifically, researchers sought to ensure that the final sample was composed of approximately 10 percent of patients who had died within 2000 and 2001, 75 percent of patients receiving ARVs, and 15 percent of patients not receiving ARVs.

For those not receiving ARVs, the study began from the end date of the sampling period and worked backwards to accommodate the most recent treatment patterns. The distribution of patients under this classification is presented in Table 2.

Table 2. Distribution of Patients under Classification

Clinical Category	Sampling Algorithm	Target % of Cases	% Cases in Sample
Deceased	Accept all cases where death occurred in the last 24 months (calendar years 2001 and 2002) until the quota was achieved	10%	10%
Receipt of ARV	Beginning with those initiating therapy December 31, 2001, and working backwards until January 1, 2000, select all cases until quota achieved	75%	78%
No ARV	Beginning from December 31, 2001, and working backwards until January 1, 2000, select all cases until quota achieved	15%	12%

5.6 Costing Approach and Assumptions

Estimates of the incremental costs of scaling up access to ARV therapies and associated care were focused on the recurrent costs directly associated with the provision of additional HIV/AIDS

services, including medications, laboratory tests, number of consultations, emergency room visits, days of hospitalization (ward and ICU), and procedures performed. Additionally, initial investments on laboratory capacity, which are of immediate interest to health sector planners in designing efforts to scale up care, were also considered.

5.6.1 Costs

Costs included the goods and services consumed for the provision of care for PLHA. To calculate total cost, resource volume and unit cost for each resource were identified.

5.6.2 Resource Volume

The study identified the volume of resources consumed corresponding to the following cost categories:

- Inpatient care: this category included length of hospital stay, emergency visits, and intensive care unit days
- Outpatient care: this included consultation costs
- Drugs: ARVs and others.
- Laboratory tests: AIDS-related (CD4, viral load, Elisa, Western Blot, culture) and non-AIDS related
- Surgical procedures and interventions

5.6.3 Unit Costs

Where available, existing unit costs for the activities identified in the previous section were utilized. The unit costs used in the study were obtained from each facility. Where the relevant unit cost was not available, an extrapolation based on the average relationship between the costs of the institution in question and another institution in the same subsystem was used to derive a cost estimate. Where this was not possible, an institution from another subsystem was used as a basis for the extrapolation and, as a last resort, private sector prices were used.

5.6.4 Diagnostic Test Costs

For most diagnostic tests, current unit cost estimates from the respective health systems were used. Cost estimates for tests of critical use in HIV/AIDS patient management—ELISA, Western Blot, CD4 count, viral load assays—were based on detailed microcosting information from a subset of study sites and considered the incremental labor, training, capital, and materials costs of these laboratory tests. In all cases the capital equipment cost was found to be zero, because the manufacturer of the diagnostic tests provides this equipment when a monthly minimum number of test kits is purchased. Thus, the capital cost is subsumed in the kit cost.

5.6.5 Calculation of Total Costs

Costs for each service delivery component were calculated by multiplying resource volume by unit costs. Total costs were calculated as a sum of service delivery component: outpatient visit costs, inpatient day costs, procedures performed, laboratory tests conducted, and drugs prescribed (both ARVs and non-ARV medications).

5.7 Study Instruments and Data Collection

5.7.1 Utilization Questionnaire (patient level)

Comprehensive data on patient sociodemographic characteristics; clinical events; use of outpatient, inpatient, and laboratory services; and use of medications were captured from medical charts using a structured computer-based interface. The interface was programmed in Microsoft Visual Basic 6 and the data stored in Microsoft Access 2000.

5.7.2 Costing Questionnaire (facility level)

Data on costing practices and the cost components of ambulatory, inpatient, and laboratory services and medications were gathered using a structured computer-based interface programmed in Microsoft Excel XP 2002. Data were gathered in the maximum degree of detail permitted by existing knowledge at each facility, and the source of each cost item (e.g., health subsystem price schedules or administrative databases, microcosting, prices for services subcontracted) was identified. Copies of instruments used are available from the authors upon request.

5.7.3 Data Collection

Five teams, each composed of two trained data collectors—one medical doctor and one economist—captured the data. Accuracy and reliability of data collection was ensured in several ways. First, the interface was designed to facilitate data collection and had automatic safeguards to prevent erroneous entries. Second, data collectors were trained for five days prior to commencing fieldwork, so as to ensure their conceptual understanding of the project and their familiarity with the instruments.

6. Study Strengths and Limitations

In comparison with previous studies of the cost of HIV/AIDS care in Latin America this study stands out for several reasons. First, unlike many studies, it does not consider the cost associated with a typical patient, but rather generates its cost estimates from a detailed review of a sample of real patients. Second, the sample size is very large, over 1000, and includes patients at multiple stages of illness (including near death), in a wide variety of health systems, at virtually all levels in the health system, in a range of different geographical settings, and cared for by a large number of different providers. Third, while no such study is able to do detailed microcosting of every aspect of care, this one advanced the state of the art in the region by performing very detailed costing of the full range of medications (and their various forms and packaging) as well as provided a detailed microcosting of the four most important laboratory tests used for diagnosis and ARV monitoring. Fourth, the inclusion of costs for 11 different sites provides not only information about cost variability within a country such as Mexico, but a sort of internal sensitivity analysis that allows data to be used in discussions with one institution while extrapolating costs from other institutions. Fifth, the study developed a real-time computerized data entry system into which users could directly enter patient information obtained from patient charts. Because this system incorporated error-checking filters, it reduced errors in the utilization data. Sixth, the study developed an innovative analytic approach, aligning patient months by initiation of ARV therapy in a way that enables a more intuitive assessment of how the cost of care changes with changes in therapy.

As with any study of this nature, there are some limitations that need to be clearly spelled out. An important characteristic of this kind of (retrospective) study is that there is no guarantee that patient records contain all the necessary and relevant information. Given the level of completeness encountered in medical records, there is no question that utilization was underestimated even within the institution studies. Furthermore, patients frequently seek care from multiple systems and providers; therefore, the medical records of a patient in any one institution will be incomplete regarding services consumed from other providers (underreporting is least likely to occur for patients who receive care from an INS and medications from the SSA). However, the primary goal was to study the change in patterns of utilization and there is no reason to believe that the introduction of HAART was associated with significant improvement in the completeness of medical records. Thus, the relative changes observed should be quite robust. The current methodology does not permit the ability to estimate the degree of underestimation in the respective study sites. To do so would require a prospective study, or at least a survey of existing patients to capture their recent utilization and compare the patient reports with the medical records.

Although the reported cost figures are believed to be conservative, the potential also exists that costs could be overestimated. For instance, the medical records, especially in the SSA institutions, contain medications and laboratory tests prescribed. Depending on the patient's financial situation, however, the prescriptions may or may not be filled. Given the dominance of ARV drug costs and the fact that SSA provides these drugs, and given that the lab tests were only included when a result was registered in the patient record, this bias is not expected to be large.

Data were collected based on the information contained in patient records in the hospitals visited. Researchers, therefore, did not track utilization by individual patients across facilities, for

example. There may have been some instances where patients were treated in two or more institutions simultaneously; in fact, anecdotal evidence does point to this happening in some cases. It is therefore likely that the full utilization of each and every patient has not been captured. However, researchers did not aim to capture the whole medical history of each patient, from the time of diagnosis to the present. Months at the end of the sample with zero utilization were discarded; i.e., the sample was truncated at the last month of utilization. This could have resulted in some overestimation of utilization rates.

The rate of hospitalization is lower than expected. This could possibly be due to the manner in which inpatient utilization is noted in medical records. The sample is biased in that only patients who had at least one outpatient visit during 2000 or 2001 were chosen. However, there may be many patients who only use the inpatient services of a given hospital, and such patients could have higher rates of hospitalization. It is also possible that there are patients who use the services of more than one hospital; in other words, a patient may not be hospitalized in the same hospital where he or she goes for outpatient visits. In this case, the inpatient utilization of these patients would not have been captured. This is true in more general rates of hospitalization as well, in that when patients receive treatment simultaneously in more than one institution, this would not be captured in the data.

The sample was not designed to be representative at the national level, but rather to reflect the situation in major treatment centers; therefore, although three very important locations were chosen for this study in terms of the number of accumulated cases of HIV/AIDS, the costs and methods of treatment may differ in other Mexican states. Additionally, the sample of patients within each hospital was not chosen randomly; rather researchers chose a proportion of patients on ARVs, patients who were not on ARV therapy, and deceased patients, so as to be able to collect meaningful data from each of these three groups. Within each of these groups, a random sample of patients met the inclusion criteria.

In terms of response to treatment, only 71 percent of the patient sample had at least one CD4 lab test result and only 69 percent had a viral load test result. Approximately 20 percent of the patients in the sample did not have these results at all. Since patients with CD4 and viral load results are probably receiving better quality care than those without monitoring test results, response to treatment of this subgroup is likely to be better than for the sample as a whole.

On the cost data side, it was not possible to do a microcosting analysis for outpatient visits and hospital bed-days. Consequently, the highest level of user fees for these two inputs was used as a proxy for costs for the SSA, INS, and ISSSTE. Despite this, costs would still be underestimated. For IMSS facilities, internal cost estimates given by IMSS were used. Specific prices for certain inputs such as drugs and laboratory tests were also not available and had to be estimated from prices for another subsystem using the average proportional difference between the two subsystems. Generally speaking, however, this only needed to be done for less common medicines and laboratory tests. It is therefore not expected that this would have led to any significant bias in the data.

One important limitation is that the reported costs do not include out-of-pocket expenditures. Since approximately 50 percent of overall medical expenditures in Mexico are out of pocket, it is likely that this would represent an important share of the total resources utilized by these patients.

As mentioned earlier, efforts are underway in Mexico to continue this area of research by undertaking an extension of data collection for the existing sample to include all of 2002; extending the sample to additional institutions, in particular to the newly certified HIV/AIDS outpatient clinics in the states; and initiating a prospective costing study in association with the creation of a

prospective clinical cohort in Mexico City. These efforts intend to address most of the study limitations cited above.

7. Key Findings

Select sociodemographic characteristics of the study sample are presented in Table 3. Key findings of this study are based on a convenience sample of patients selected from each of the three health subsystems in Mexico. Although the sample was designed to capture a sufficient number of patients both using and not using ARV therapy, those patients were randomly selected within the sample stratification. It is believed that the sample size is sufficiently large to yield a population that is reasonably representative of the national population and of PLHA in regards to nonstratification variables. The figures on educational attainment, mode of HIV transmission, and sexual preference found in Table 3 support this hypothesis and raise confidence that study results can be used to make inferences about PLHA who seek care at various facilities within the three health subsystems.

The sample population is primarily male (70.4 to 83.5 percent), as is the case with the general PLHA in Mexico (84 percent). Similarly, the principal mode of transmission is sexual (94.3 to 95.8 percent in the study sample, 89.8 percent in the PLHA), and the epidemic is concentrated among men who have sex with men (59.1 percent in the INS, 59.6 percent in the SSA, and 61 percent in the PLHA). Social security is an exception with 61.7 percent of respondents identifying themselves as heterosexual. This difference in sexual preference noted at the IMSS/ISSSTE is statistically significant. Authors speculate that there may be bias in reporting of sexual preference, particularly in the social security hospitals, because social security coverage is employment based; however, this line of inquiry was not pursued since it is outside the purview of this study.

The education level of the IMSS/ISSSTE sample population is also statistically significantly different from the sample averages for the other subsystems, which in turn are similar to the national average. Relative to the national average, a much lower percentage of IMSS/ISSSTE patients, 9 percent compared with 28.2 percent nationally, completed primary education or less, while a much higher percentage, 38.2 percent compared with 12.1 percent nationally, reached the university level. This is not unique to PLHA seeking care in social security facilities. It probably reflects the premise that an insured population, by the nature of its formal sector employment, is more likely to be educated.

Table 3: Characteristics of 1062 HIV+ Individuals in the Mexican Public Health Sector, by Health Subsystem

		Ministry of Health (SSA) (n=653	Social Security (IMSS/ ISSSTE) (n=294	National Institutes of Health (INS) (n=115)	National Average
	No. of facilities	*5*	*4*	*2*	
Sex, male (%)		83.46	81.29	70.43	
	Min/Max	*57.14-91.89*	*76.06-91.49*	*65.71-77.78*	
Schooling (n)		506	144	87	
		76%	*49%*	*76%*	
Primary or less (%)		30.0	9.0 *	26.4	28.2 (a)
	Min/Max	*15.29-50*	*2.86-13.04*	*8.33-33.33*	
Preparatory or less (%)		54.0	52.8 *	55.2	51.8 (a)
	Min/Max	*39.13-65.38*	*28.57-72.41*	*50.00-57.14*	
Higher education (%)		16.0	38.2 *	18.4	12.1(a)
	Min/Max	*7.41-22.31*	*17.65-68.57*	*9.52-41.67*	
Transmission mechanism (n)		496	175	69	
		75%	*60%*	*60%*	
Unsafe injection (%)		1.21	0.00	0.00	0.9
	Min/Max	*0-5.56*			
Transfusion (%)		3.02	5.71	2.90	8.7
	Min/Max	*0-11.43*	*0-10.42*	*2.7-3.13*	
Occupational Risk (%)		0.00	0.00	1.45	0
	Min/Max			*1.45-3.13*	
Sexual (%)		95.8	94.3	95.7	89.8
	Min/Max	*88.57-100*	*89.58-100*	*93.75-97.3*	
Sexual Preference (Males: 85% of all people who had been sexually transmitted)		404	127	44	
		61%	*43%*	*38%*	
Heterosexual, male (%)		40.3	62.2 *	40.9	39 (b)
	Min/Max	*32.7-57.14*	*53.13-70.83*	*40.91-40.91*	
Homosexual, male (%)		45.5	29.9 *	43.2	36 (b)
	Min/Max	*10-54.03*	*25-37.5*	*36.36-50*	
Bisexual, male (%)		14.11	7.87 *	15.91	25 (b)
	Min/Max	*7.14-50*	*4.17-9.38*	*9.09-22.73*	

Note: P values compare IMSS/ISSSTE to SSA and to INS using chi square tests. * *P* <.001.

Sources

(a) INEGI (s/f) *Estadísticas sociodemográficas - Indicadores sobre características educativas de la población,* *Y* . Available at: http://www.inegi.gob.mx/difusion/espanol/fiest.html . *National averages.*

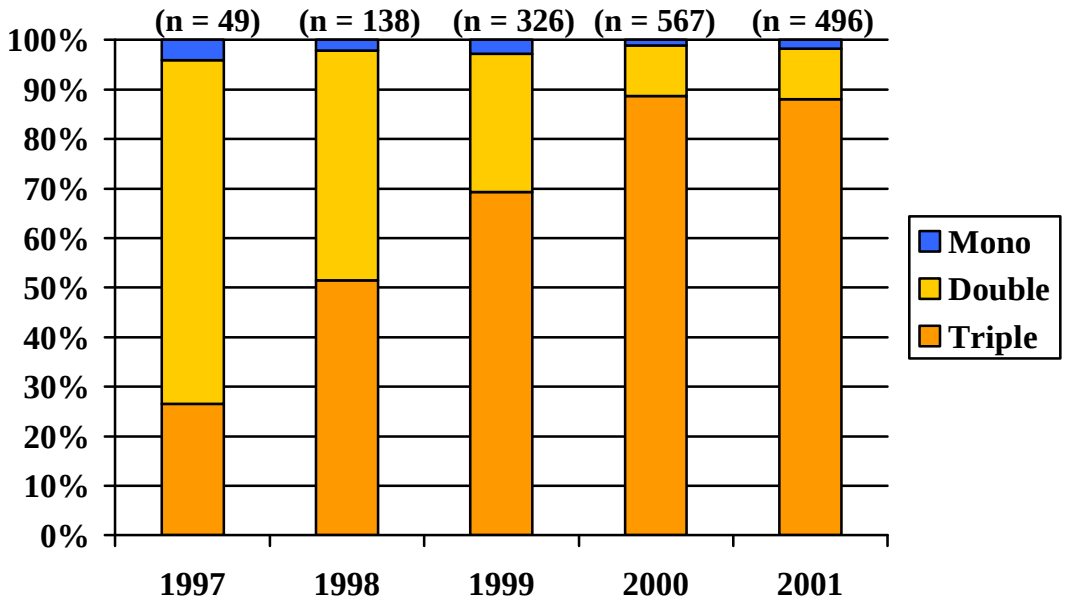
(b) CENSIDA (2002) *Panorama Epidemiológico del VIH/SIDA e ITS en México.* Cuadro 5 - Casos nuevos y acumulados de SIDA en personas de años y más, según categoría de transmisión. México, -2001. Available at: http://www.ssa.gob.mx/conasida/estadis.htm. *PLWA averages.*

The following paragraphs highlight key study findings.

There has been a progressive and rapid move towards triple therapy[4]

In 1997, 69.4 percent of patients receiving ARVs were on double therapy and only 26.4 percent were on triple therapy. By 2001 the vast majority of patients (88.1 percent) were on a three-drug regimen, while the share of double therapy recipients had dropped to 10.1 percent. The number of patients on monotherapy had also decreased steadily, though a small number of patients remains on a single medication despite treatment guidelines that recommend triple therapy as the norm and double therapy in exceptional cases (see section 3.2). Figure 1 shows this rapid move towards triple therapy.

Figure 1. Distribution of Patients by Type of Therapy



As Table 4 shows, the uptake of triple therapy varied across subsystems, with first the SSA and then the INS adopting current standards more quickly than IMSS/ISSSTE. This may be explained by the fact that fewer patients were ever on double therapy in the SSA and INS subsystems. The SSA and INS samples are skewed toward later initiation dates due to the lag in coverage for ARV treatment for the uninsured compared to the insured population (see section 3).

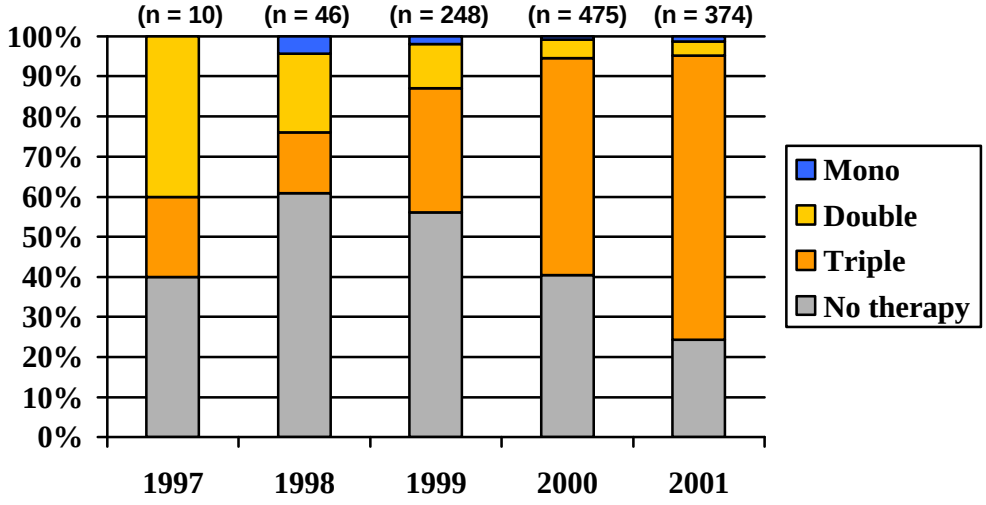
[4] Triple therapy is used as shorthand for triple drug combinations using either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor with two nucleoside/tide reverse transcriptase inhibitors. The term is used interchangeably with HAART.

Table 4. Percentage of Patients Receiving Triple Therapy Among Those Receiving Any Therapy, by Subsystem

Calendar year (n=patients on any therapy)	Triple therapy		
	SSA	IMSS/ISSSTE	INS
1997 (n_{SSA}=6, $n_{IMSS/ISSSTE}$=40, n_{INS}=3)	33.3%	25.0%	33.3%
1998 (n_{SSA}=18, $n_{IMSS/ISSSTE}$=91, n_{INS}=29)	38.9%	50.5%	62.1%
1999 (n_{SSA}=109, $n_{IMSS/ISSSTE}$=168, n_{INS}=49)	70.6%	68.5%	69.4%
2000 (n_{SSA}=283, $n_{IMSS/ISSSTE}$=208, n_{INS}=76)	90.8%	85.6%	89.5%
2001 (n_{SSA}=283, $n_{IMSS/ISSSTE}$=167, n_{INS}=46)	93.6%	78.4%	89.1%

The sample selection criteria (see section 5.5) does not allow much to be said about the probability of receiving or not receiving ARV treatment across subsystems. Further, the facilities studied were chosen because they offer triple therapy. They are not typical of facilities nationwide, and an extrapolation based on these figures would significantly overestimate coverage. With these caveats in mind, it is interesting to note that while there is little variance across the study period in the share of patients not receiving ARVs in the INS and IMSS/ISSSTE, that does not hold true in the SSA, where up to 60 percent of patients were not on ARV treatment in 1998 (see Figure 2). These figures confirm the perception that the uninsured lacked access to treatment in the late 1990s.

Figure 2. Distribution of SSA Patients by Type of Therapy



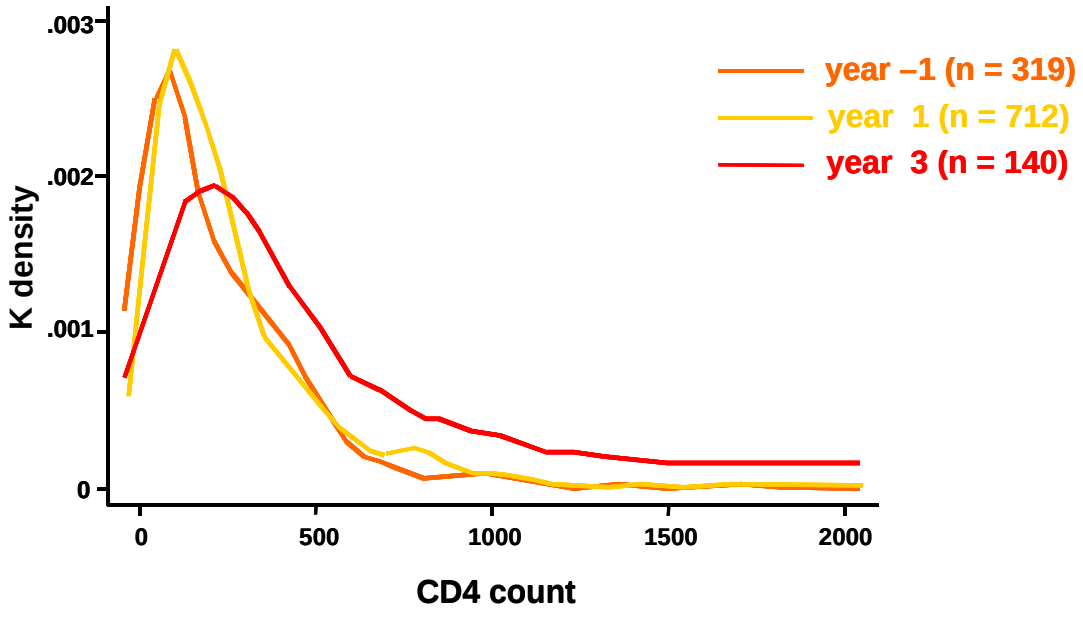
Patients start treatment in advanced stages of illness and improvement is gradual

For this analysis, patients were lined up according to the date of initiation of triple therapy, so Year 1 refers to the 12-month period following that date and Year -1 is the 12-month period prior to initiation of triple therapy. Through this methodology, the five-year period covered by the study (1997-2001) generates data up to five years on either side of the initiation date of HAART (Year -5 to Year 5). However, due to the small n at the endpoints of the distribution, the reporting of findings will be restricted to an analysis of data for Year -3 to Year 3 (see Table 5).

Table 5. Patient-year Distribution by Year Pre- and Post-HAART

Year	n
-5	1
-4	12
-3	45
-2	153
-1	612
1	792
2	459
3	201
4	50
5	10
Total	*2335*

Figure 3. Distribution of CD4 Count



Data from the study confirm the commonly held belief that initiation of triple therapy treatment in Mexico occurs only once patients are very ill. Despite norms that state that double therapy should only be used when the CD4 count exceeds 350 cells/mm^3, in the year leading up to initiation of triple therapy the median CD4 count was well below that, at 150 cells/mm^3. Furthermore, in Year -1 there is a high concentration of patients around the median, indicating that a large number of patients who likely qualify for triple therapy are receiving either double, mono, or no ARV therapy. (See Graph 3 for a distribution of the CD4 count.)

Once again, there are notable differences across subsystems. Patients are started on triple therapy earlier in the IMSS/ISSSTE (median CD4 = 255 cells/mm^3 in Year -1), followed by the INS (196), and then the SSA (111). Readers should exercise caution in interpreting these results because the CD4 values being compared were obtained from different labs. Even for a given patient, tests conducted in different labs tend to produce varying results.

There is substantial benefit of therapy as indicated by the surrogate marker CD4. Although improvement in CD4 counts is gradual, with the median rising to 292 cells/mm^3 in Year 3 from 180 cells/mm^3 in Year 1, the rate of improvement is in line with what would be expected since patients on triple therapy generally have an average CD4 increase of 75 to 100/mm^3 per year. During the three years after initiation of triple therapy, there is wider variance in CD4 levels across patients, with some patients responding well while others do not.

Less than half of all patients in each of the subsystems have records that document results for both ELISA and Western blot, which are the recommended norms for screening and confirmation tests, respectively. Interviews with providers indicate that these figures most reveal that there is incomplete documentation of results of AIDS tests.

Table 6. Record of Confirmation of Diagnosis of HIV Infection

	Ministry of Health (SSA)	Social Security (IMSS/ ISSSTE)	National Institutes of Health (INS)	Total
Diagnostic test	**(n=653)**	**(n=294)**	**(n=115)**	**(n=1062)**
ELISA	268	86	39	393
Western blot	6	18	3	27
Culture	3	0	0	3
ELISA + Western blot	272	133	37	442
Other	86	54	36	176
None	18	3	0	21
Total	653	294	115	1062

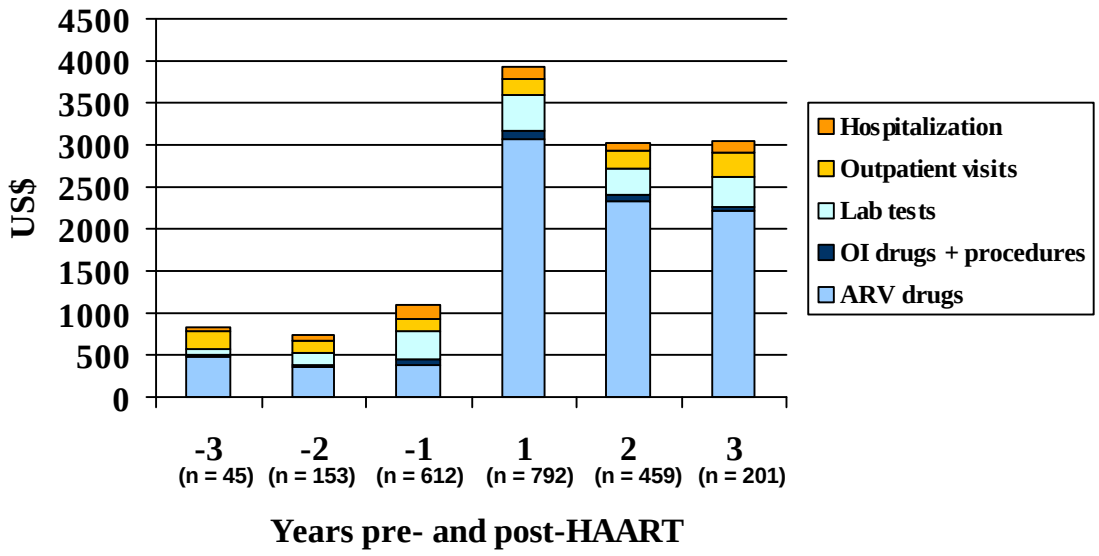
Total costs are substantially higher under triple therapy

As Figure 4 indicates, there is a marked increase in the average annual cost per patient after initiation of triple therapy. This is primarily due to the cost of ARVs. These drugs are the single largest cost component throughout the study period, but their contribution to total cost jumps significantly once patients are started on triple therapy. Pre-HAART, ARVs account for 35.2 to 59.4

percent of total costs, whereas their share increases to 72.7 to 78.3 percent of total costs post-HAART.

It is important to clarify that changes in the average cost per patient are explained solely by differences in resource utilization. The unit cost of resources, such as ARV and OI drug prices, was held constant in 2002 pesos.[5] This method was applied because the purpose of the study was not to investigate changes in treatment cost over time but rather to make inferences about the relative costs of specific treatment categories and to estimate the total cost of ARV treatment programs.

Figure 4. Average Annual per Patient Cost of Treatment, by Years Pre- and Post- HAART

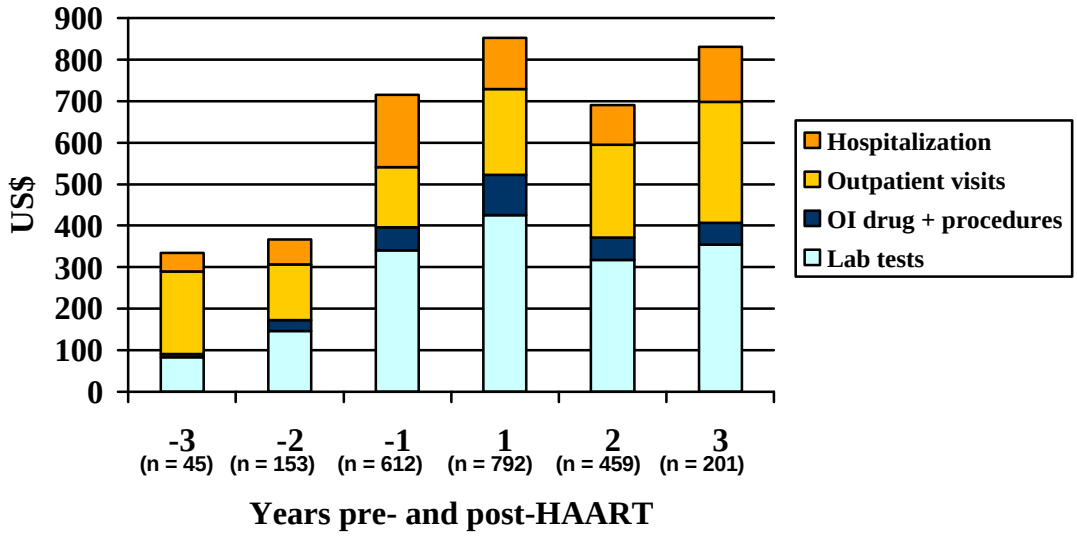


Another interesting finding from Figure 4 is that there is a significant drop in cost per patient in the second year after initiation of HAART. The authors speculate that this drop may be due to drug intolerance or lack of compliance. However, the exact reasons behind the drop in utilization of ARVs cannot be ascertained, as this information is generally not specified in patient records. To obtain such information would require a prospective study where patients would be followed through periodic interviews, allowing researchers to collect data on patients even if they drop out or move across subsystems. An analysis of compliance is further hindered by the fact that patients are only required to visit a doctor every three months; in between visits, patients are allowed to fill their prescriptions directly at the pharmacy. Patient records do not reflect whether the prescription was actually filled. In this study, ARV utilization was extrapolated for three months. If no outpatient visit occurred after three months, then resource volume for ARVs was estimated to be nil.

A closer look at costs for items other than ARV drugs reveals some interesting patterns (see Figure 5). Lab tests, which account for 10 to 31 percent of total ARV per patient costs, do rise substantially in Year -1. However, initiation of triple therapy has little effect on lab cost because the increase in the AIDS test is partially offset by a decline in non-AIDS-specific tests.

[5] Exchange rate: US$1 = 9.67 Mexican pesos in 2002 (http://www.banxico.org.mx/).

Figure 5. Average Annual per Patient Cost Treatment Excluding ARV Drug Costs, by Years Pre- and Post-HAART



Outpatient visits are the second largest contributor to treatment costs, excluding ARVs

The number of outpatient visits rises once patients are on triple therapy. Although patient records do not distinguish between monitoring visits and those for treatment of opportunistic infections (OIs), the drop in costs for OI drugs post-HAART supports the conclusion that the increase in outpatient visits is attributable to the monitoring of ARV treatment. Patient records also do not generally assign a diagnosis to the patient, so it was not possible to disaggregate treatment cost per OI. A review of drugs prescribed indicates that the most commonly found OIs in the study sample were: oral candidiasis, Kaposi's sarcoma, and herpes zoster (see Table 7).

Table 7: Most Commonly Occurring Opportunistic Infection in the Sample

Opportunistic infection	N
Oral candidiasis	405
Kaposi's sarcoma	380
Herpes zoster	263
Cerebral toxoplasmosis	236
Pulmonary tuberculosis	206
Pneumonia (pneumocystis carinii)	171
Candidiasis orofaringea	135

A somewhat surprising factor, given what is known about AIDS patients in other developing countries (Guinness et al. 2002), is that hospitalization costs are not a major factor. In Mexico, hospitalization represents less than 10 percent of total costs in any given year, with the exception of Year -1, where its share reaches a high of 15.8 percent. This is due to the low utilization of this expensive service. Average hospital days do drop slightly post-HAART, but the drop is not enough to compensate for the rise in ARV costs.

Table 8. Average Annual per Patient Utilization of HIV/AIDS-related Services, by Years Pre- and Post-HAART

	Outpatient visits		Hospital days		Non AIDS-specific tests		AIDS tests	
Year	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation
-3 (n=45)	5.7	4.8	0.7	7.9	2.7	5.0	1.0	1.6
-2 (n=153)	4.6	5.5	1.2	8.4	4.6	10.3	1.4	3.1
-1 (n=612)	6.3	6.2	2.2	10.0	11.1	23.2	2.2	3.7
1 (n=792)	10.3	5.7	1.9	6.5	11.4	18.3	2.8	2.9
2 (n=459)	8.9	5.1	1.3	7.0	7.9	19.3	2.3	2.5
3 (n=201)	10.0	4.6	1.5*	7.0	8.6	18.8	2.6	2.7

*If two outliers with high utilization of hospital days are removed the mean drops to 0.6.

In summary, there is no immediate cost savings from the initiation of triple therapy. The cost of ARVs, which is high from the start, rises substantially, but the decline in the use of inpatient services is too small to make a difference. While the impact of triple therapy on the utilization of lab tests is mixed, lab costs do go up, as do costs for outpatient visits. The cost of OI drugs and procedures do drop, but the impact on total cost is negligible.

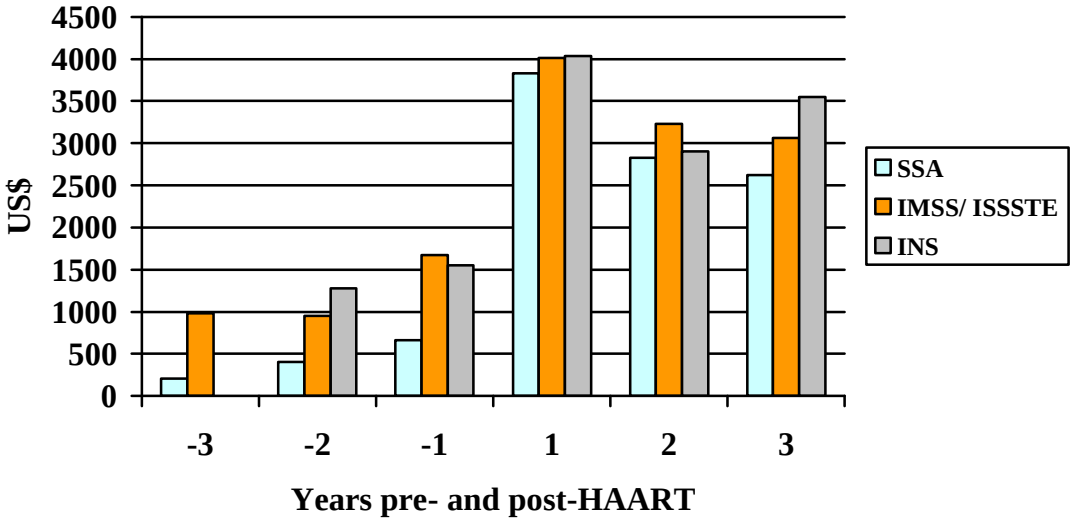
Furthermore, the data presented here only cover three years of triple therapy. Evidence from Brazil (National Coordination for STD and AIDS, Brasilia 2000), as well as anecdotal evidence from provider interviews, suggests that the average lifespan of patients on HAART is approximately 60 months. There is reason to believe that costs are high as patients approach death. For this reason, investigators over-sampled patients who passed away during the study.

Cost vary across subsystems

The cost patterns discussed above are replicated uniformly across the various subsystems.[6] There is a marked increase in cost after initiation of triple therapy, and ARVs are the major contributing factor to this increase. Costs are higher in the IMSS/ISSSTE and INS subsystems as compared to the SSA.

[6] The increase in INS costs in Year 3 is due to an outlier that spent 12 days in intensive care, significantly raising the unit cost of hospitalization in the INS for that year.

Figure 6. Average Annual per Patient Cost of ARV Treatment by Subsystem and by Years Pre- and Post-HAART*



*Note: Sample sizes are presented in graphs 7-9. INS figures for Year –3 were dropped from the analysis by subsystem due to the small sample size.

Figures on the total cost per patient (see Figure 6) mask some important differences across subsystems. For instance, the SSA and INS spend more on lab tests—both as a share of total spending and in absolute terms—than the IMSS/ISSSTE. Conversely, a significantly larger share of IMSS/ISSSTE total costs is associated with the provision of outpatient services and these costs jump by 27.5 percent the year after initiation of HAART. This, along with the fact that OI drug costs do not vary significantly over the study period, indicates that IMSS/ISSSTE patients are receiving more monitoring visits then their counterparts in the SSA and INS.

Figure 7. Average Annual per Patient Cost of Treatment Excluding ARV Drug Costs in the SSA, by Years Pre- and Post-HAART

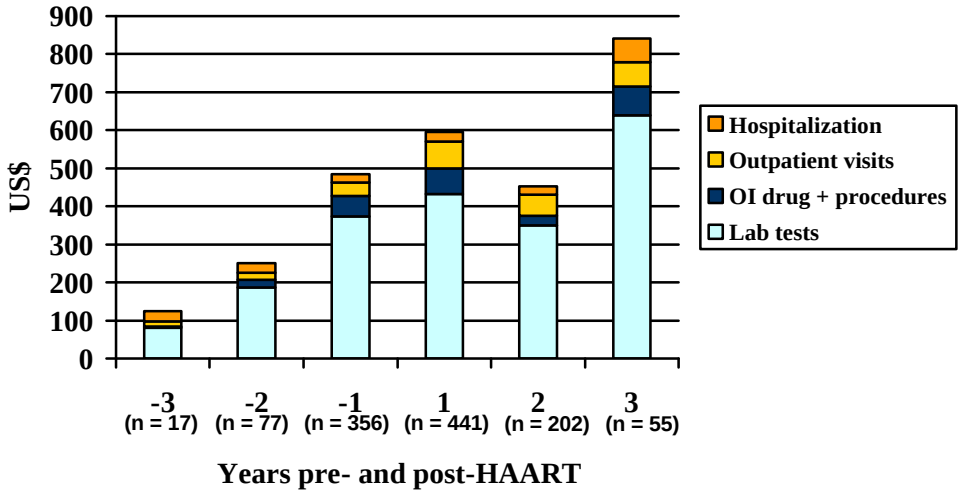


Figure 8. Average Annual per Patient Cost of Treatment Excluding ARV Drug Costs in the IMSS/ISSSTE, by Years Pre- and Post-HAART

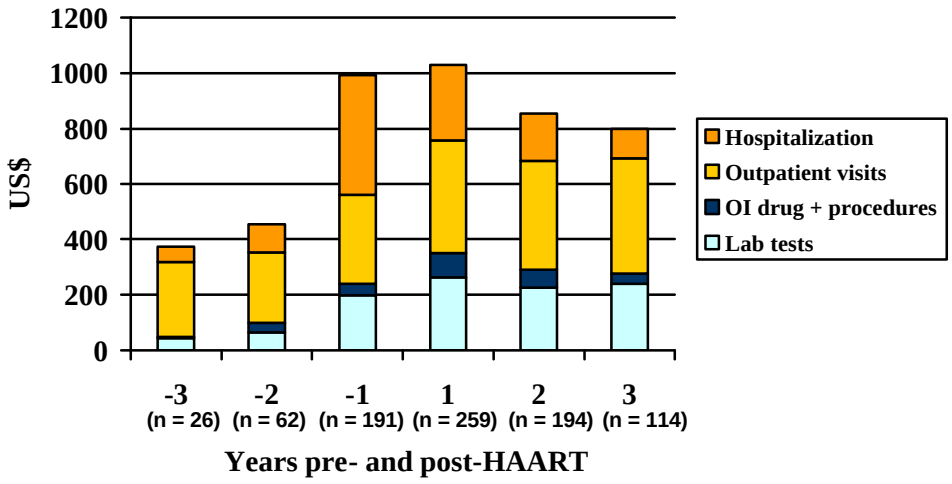
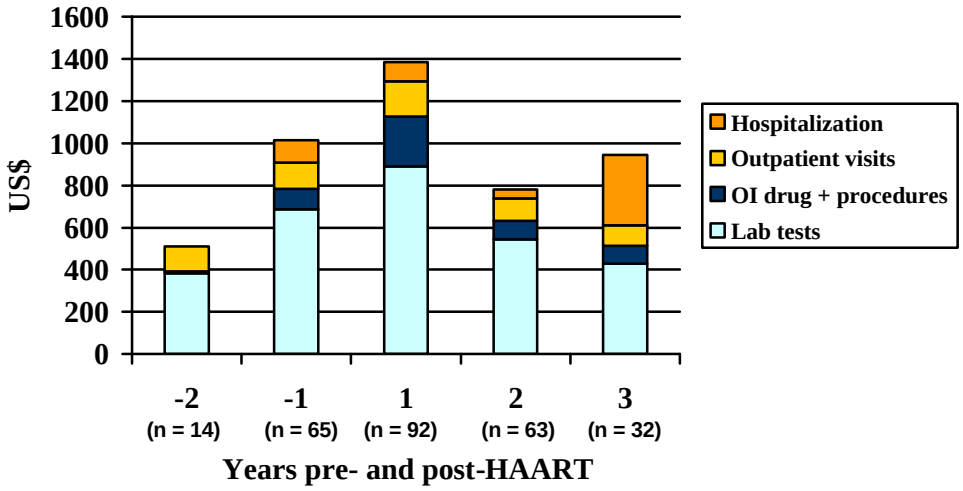


Figure 9. Average Annual per Patient Cost of Treatment Excluding ARV Drug Costs in the INS, by Years Pre- and Post-HAART



Most of the variation that does exist across subsystems in non-ARV costs is driven by differences in utilization (see Table 9). This is the case for outpatient visits, where utilization is higher in the IMSS/ISSSTE, as well as for lab tests, where utilization is higher in the SSA and INS. The exception is in hospitalizations. Hospitalization costs are higher in the IMSS/ISSSTE, although utilization patterns are similar to those found in the INS and only slightly lower than those of the SSA. Higher unit costs for hospitalization in the IMSS/ISSSTE explain why total hospitalization costs in the social security system exceed hospitalization costs elsewhere.

Table 9. Average Annual per Patient Utilization of HIV/AIDS-related Services, by Year Pre- and Post-HAART by Subsystem

	Outpatient visits			Hospital days			Non AIDS-specific tests			AIDS tests		
Year	SSA	IMSS/ ISSSTE	INS	SSA	IMSS/ ISSSTE	INS	SSA	IMSS/ ISSSTE	INS	SSA	IMSS/ ISSSTE	INS
-3	1.7	6.9	- -	2.0	0.3	- -	4.7	1.4	- -	0.9	0.7	- -
-2	2.0	6.8	6.9	2.0	0.6	0.0	5.6	3.2	7.1	1.6	0.7	4.1
-1	4.3	8.9	7.8	1.6	2.7	4.2	12.3	7.3	18.0	2.7	1.1	3.3
1	9.0	11.7	11.4	1.9	1.8	2.3	12.8	6.5	20.2	3.0	2.1	4.7
2	6.9	11.1	7.0	1.6	1.0	1.1	9.8	5.2	11.6	2.4	1.9	3.0
3	7.8	11.6	6.6	4.7*	0.7	0.7	21.2**	4.7	7.6	3.6	2.1	3.4

*If two outliers with high utilization of hospital days are removed the mean drops to 1.5.
**It is very likely that this jump is explained by two outliers in the sample. One of has more than 100 tests and the other more than 60. If the outliers are removed, the mean drops to 8.3.

Treatment costs are higher for patients in advanced stages of illness

Excluding ARVs, the average cost of treating patients with CD4 counts below 200 cells/mm^3 is approximately 30 percent higher than for other patients (see Table 10). Higher costs are due to a near doubling of the number of days spent in a hospital as well as greater use of non-AIDS specific diagnostic tests (see Table 11). These findings suggest that there are cost implications of waiting until patients are very ill before initiating triple therapy. As the health of the patient worsens, associated treatment costs increase. This is probably due to the occurrence of OIs, which is likely to explain the rise in utilization of hospital days and non-AIDS laboratory tests.

Table 10. Average Annual per Patient Cost of Treatment Excluding ARV Drug Costs, by Stages of Illness

CD4 range	Outpatient visits	Hospital days	Lab tests	OI drugs + procedures	Total
0-199 (n = 1016)	190	104	759	91	1144
200-349 (n = 484)	205	36	603	30	874
350-499 (n = 270)	279	23	565	21	888
>500 (n = 306)	271	8	496	61	836

Table 11. Average Annual per Patient Utilization of HIV/AIDS-related Services, by Stages of Illness

CD4 range	Outpatient visits	Hospital days	Non AIDS-specific tests	AIDS tests
0-199 (n = 1016)	10.1	3.3	20.1	5.6
200-349 (n = 484)	9.8	1.7	13.1	5.1
350-499 (n = 270)	10.3	1.8	10.8	6.1
>500 (n = 306)	11.1	0.6	10.0	5.3

Treatment costs are higher for patients in their last year of life

Treatment costs are also higher during the last year of a patient's life (see Table 12). Excluding ARVs, treatment costs are two to three times higher for patients near death than for the average patient. As with patients in the advanced stage of illness, those in the year preceding their death spent more time in the hospital and were submitted to a greater number of non-AIDS specific tests.

Furthermore, the longer patients were under treatment, the higher the costs during the last year of life (see Table 13). As with the analysis on stages of illness, higher costs are associated with increases in hospitalizations and the use of non-AIDS tests, probably due to a rise in OIs. Because the n values are low, this line of analysis would require further research.

Table 12. Average Annual per Patient Cost of Treatment Excluding ARV Drug Costs, During Last Year of Life

Year	Outpatient visits	Hospital days	Lab tests	OI drugs + procedures	Total
-1 (n = 23)	152	917	491	108	1668
1 (n = 51)	189	732	699	273	1893
2 (n = 30)	204	1002	643	244	2092
3 (n = 13)	296	795	1111	251	2452

Table 13. Average Annual per Patient Utilization of HIV/AIDS-related Services, During Last Year of Life

Year	Outpatient visits	Hospital days	Non AIDS-specific tests	AIDS tests
-1 (n = 23)	6.2	9.7	22.9	1.6
1 (n = 51)	10.7	8.3	24.2	3.2
2 (n = 30)	9.3	9.8	27.9	3.0
3 (n = 13)	10.0	18.4	46.6	2.7

These findings confirm that there is a concentration of costs at the end of life. ARVs prolong life, postponing the burden of hospitalization and other treatment costs. The total cost to the health system of providing HAART therapy will vary depending on the lifecycle of patients receiving treatment.

8. Discussion

Given the rapid recent increase in the provision of ARV care for PLHA in Mexico, researchers expected to encounter in this study evidence of large concerted efforts to train medical staff in HIV care and efforts to increase laboratory capacity. Instead they found the opposite in the health facilities studied. Although isolated efforts to provide some training were encountered (for example, when the Clinica Condesa first started operations, it conducted some sensitivity training sessions to help its staff provide appropriate care for marginalized populations), the majority of medical staff learned to care for PLHA through informal, self-taught or collegial mechanisms. Likewise, increases in laboratory capacity have also been the result of multiple, informal efforts. For example, in Guadalajara, all three of the large public hospitals contract out their viral load tests to the local private sector. In Cuernavaca, hospitals buy the services from their affiliated hospitals in nearby Mexico City. As a result, costs for training or for increasing laboratory capacity have not been included in this report.

However, not including these costs does not suggest that they are inappropriate costs to consider in countries dealing with scaling up of ARV coverage. Surely the great heterogeneity in practice patterns encountered in this study is partly the result of the lack of organized training of medical personnel. Just as Mexico is now considering mechanisms to improve the quality and consistency of its ARV care, other countries should consider building such mechanisms in from the beginning.

In this study, two different approaches were used to generate unit costs. For the most important cost categories, namely drug costs and the cost of ARV-associated monitoring tests, researchers performed a microcost analysis, reviewing the primary purchasing data in the case of drugs and conducting a detailed analysis of the relevant laboratory procedures (Gasca et al. 2003). For the remainder of the unit costs (cost per bed day, cost per visit, procedure costs, etc.), the facility-specific unit cost estimates provided by the facility were used. This latter approach is clearly inferior to microcosting because the facilities generate estimates for accounting purposes rather than to inform economic analyses, but given the study's time constraints and financial limitations, it was not feasible to consider performing a full microcost analysis of all services patients with HIV/AIDS received in these facilities. As additional studies improve the precision of these unit cost estimates, it will be possible to re-estimate total cost estimates in the models.

Capital costs for drugs were not considered in this study, as they were not believed to be significant (the incremental costs for storage, for example, were negligible). Incremental capital costs were considered for laboratory tests. Thus, the cost of the viral load analyzer is considered, as it is subsumed in the test kit cost; the attributable cost for the space utilized in the general laboratory refrigerator is not considered. Capital costs are considered to varying degrees in the unit costs provided by the various health facilities, but those methodologies are not transparent. However, given that the intersite variation that is explained by differences in non ARV-related utilization is relatively small, the likelihood that differences in treatment of capital costs is important is remote.

ARVs constitute the largest proportion of costs for HIV patients, and should in fact be even larger if the fact that the data in all likelihood underestimates ARV utilization is considered. The Mexican government, like all governments in developing countries facing large costs for the

treatment of HIV/AIDS, is very concerned about the cost of ARVs and is exploring a number of responses. It has already undertaken multiple rounds of negotiations with pharmaceutical manufacturers and has achieved important reductions in the cost of many ARVs. However, Mexico has achieved far less success in this area than countries such as Brazil, India, Thailand, and South Africa that have either developed a domestic ARV production capacity or openly considered the possibility.

Table 14 shows that, for the most part, ARV prices in the public sector in Mexico are lower than those in the United States. Mexico has benefited from its developing country status in terms of being eligible for certain price reductions granted by pharmaceutical companies. The Ministry of Health also recently negotiated a deal with Merck for a reduction in the price of Indinavir and Efavirenz, and will continue to attempt to "find other alternatives to reduce the cost of ARVs and other medicines." (CENSIDA 2002)

Table 14. Antiretroviral Price Comparison, May 2001 (in US$)

	Mexico	Brazil	Argentina	USA
Didanosine 100mg	0.87	0.50	0.45	---
Efavirenz 200mg	0.89	2.32	4.29	3.94
Lamivudine 150mg	3.40	0.81	0.25	4.15
Lamivudine 150mg + Zidovudine 300mg	5.10	0.70	0.67	8.99
Nelfinavir 250mg	1.78	1.36	0.97	2.02
Nevirapine 200mg	2.98	---	0.84	4.38
Saquinavir 200mg	0.83	---	1.10	1.14
Staduvine 40mg	2.58	0.27	0.11	4.51
Zidovudine 250mg	0.22	0.18	0.15	1.61

Source: PAHO, 2001

Another clear study finding is that ARVs are not cost saving. In the first place, total utilization increases once patients begin taking ARVs. Although study results show a decline in hospital days after patients begin triple therapy, this decline is not nearly large enough to offset the increase in costs attributable to ARVs. This is inconsistent with data from a Brazilian study which showed that ARVs actually have a cost-saving effect due to the sharp decline in annual AIDS-related admissions per patient following the introduction of HAART (Ministry of Health (Brazil) 2003). Furthermore, the effect of ARVs is to prolong life, postponing the burden of hospitalisation costs.

Despite the above-mentioned bias in the sample, which could have led to an underestimation of utilization of inpatient services, an interesting trend can be observed in the hospitalization data. The highest rate of utilization of inpatient services occurs in the 12 months before patients start triple therapy. This suggests that most patients begin therapy when they are already at a very advanced stage of the disease. The median CD4 count during this period is 150 cells/mm^3 with a mean of 223 cells/mm^3. The point recommended for the initiation of ARV therapy in the latest guidelines is between 200-350 cells/mm^3. Late initiation of ARV therapy may result in a less-than-optimal response to treatment (WHO 2002). It is likely that a combination of factors is responsible for this occurrence. Some patients may not know their HIV status until they develop a serious opportunistic infection and have to be hospitalized. Other patients who know their HIV status may not seek

treatment for their condition until very late, possibly because they are in denial of their illness. A further reason could be that doctors are not following the official norms and only prescribe ARVs when the patient is seriously ill. In addition, access to triple therapy was not widespread until recently.

Adherence to ARV treatment seems to be an important problem, with many patients leaving therapy. There are two possible reasons for this. One is that the supply of ARVs is inadequate: patients may be forced to stop their medication because of stock-outs in the hospital pharmacy. The extent of this problem is not fully known, but there have been reports in the press of supply shortages in IMSS and ISSSTE hospitals. A second reason is that the patient may choose to stop taking the medication. Some patients experience side effects from ARVs, while others may decide to stop treatment when they are feeling better.

Another clear policy finding is that no institution completely follows the normal procedures for treatment, despite the fact that these norms are “official” and supposedly obligatory. Inconsistent patterns of treatment suggest important room for quality improvement, independent of the purchase of drugs. In many cases, the treating doctor prescribes a regimen that reflects his or her personal beliefs about what is best for the patient, rather than a regimen that follows the official norms. Furthermore, the official norms are not updated regularly enough to reflect the most recent advances in technology and knowledge. The current norms, for example, were developed in 2000, and although, as previously mentioned, a new version has been formulated, this new version has not yet been made official.

9. Conclusions and Recommendations

Mexico's experience has shown that the *cost and feasibility* of providing HAART to PLHA is operationally feasible. In Mexico, the costs of the ARV medications and the associated monitoring are in the range of one to two times per capita GDP at current prices, depending on the setting in which care is delivered. This annual expense, however, is clearly not competitive with the most cost-effective health interventions supported by the public sector in Mexico, nor is it among the least cost-effective. It should be noted that this analysis did not take into account any of the postulated positive externalities of providing care that could increase the effectiveness of prevention efforts, nor did it consider the benefits, individual and societal, of PLHA rejoining the labor force. To the extent that these positive externalities are significant, investment in HAART will be more cost-effective than it appears here. The study clearly shows that the cost of the ARVs is by far the most important cost component of providing HAART and thus the ability to negotiate lower drug prices remains the key to improving the cost-effectiveness of HAART. The study also shows that costs of other methods of HIV/AIDS care drop once HAART is initiated, but by a far smaller amount than the increase in costs associated with providing HAART. Thus, the study did not confirm previously published reports from both Mexico and Brazil suggesting that HAART can actually be cost saving[7].

The enormous observed *variability in patterns of care* and the sporadic adherence to official norms and guidelines suggest that there is much room for improvement in the effectiveness of HIV/AIDS care, even at current funding levels. Further investigation is necessary to understand which are the most important determinants of this variability: How often do physicians not have sufficient resources at their disposal to provide the level of care set out in CENSIDA's guidelines? How important is insufficient physician training and experience in the treatment of HIV? What role does the management of the different subsystems, or individual institutions, play either in creating incentives or in implementing quality assurance procedures? How would behavior change if providers were less ignorant of the literature or less ignorant of how their own practice pattern differs from that of their colleagues? What role is patient preference playing in determining prescribing patterns? What influence does the black market for ARVs have? Among these questions, the authors would place highest priority on investigating provider knowledge and revealing practice pattern variations among physicians. The former could be done at modest expense using clinical vignette methodology (Peabody, Gertler et al. 1994, Peabody, Gertler et al. 1998), and dissemination of the results of this study could prove a useful first step in providing feedback to providers on clinical practice variation. It would also be useful to model the impact on cost and effectiveness of this variability in care patterns. Price reductions on selective ARVs in Mexico creates the opportunity for greater inefficiency in prescribing appropriate drugs, and modeling may show that improved training and management could be cost saving.

Another important finding is that *patient adherence* to ARV regimens appears to be poor in all subsystems. While the retrospective nature of the study makes it difficult to distinguish between poor medical recordkeeping and poor adherence, the authors were conservative with respect to coding

[7] The authors must stress that the conclusions drawn from this study must be taken with caution considering that they refer to the study sample.

adherence failure, assuming that patients continued their therapy for three months following their last visit. Thus, it is likely that adherence may be worse than reported. One potential mitigating factor mentioned previously is that the study only follows a patient's experience in one health facility. To the extent that some patients receive care in more than one facility, some patient adherence may be underestimated. The importance of maintaining very high levels of adherence to achieve clinical effectiveness of HAART has been well documented (Hogg et al. 2001, Paterson et al. 2000). Because of the highly nonlinear relationship between adherence and effectiveness, expansion of public sector provision of HAART is likely to be extremely inefficient at low levels of adherence. Instead, the public sector could reprioritize its actions and dramatically improve adherence for a smaller number of patients.

As with practice variation, further investigation into the causes of poor adherence is warranted. Although many of the root causes may be similar to those previously cited (insufficient resources or stock outages, poor provider training, poor management, or poor quality control), patient characteristics surely play an important role. Socioeconomic differences among patients in Mexico are even more pronounced than they are in the United States, with a far larger proportion of patients living in extreme poverty. The research institutes of the Ministry of Health have made it their priority to research the determinants of poor adherence and the effectiveness of approaches to improve adherence. Extending the present study to include patient interviews would be a useful way to better understand the factors involved in patient adherence and in assessing the importance of incomplete medical records. In parallel, one could compare approaches for improving adherence such as improving physician training, providing better social support for patients, and initiating directly observed treatment.

Monitoring the patient's response to ARV therapy (through CD4, viral load, and viral resistance) is an area that relates both to variation in practice patterns and to adherence. In this area lessons from clinical experience in wealthy countries are more difficult to translate to the Mexican setting. As drug prices fall in developing countries, monitoring costs become a larger proportion of total costs. This results in a natural tendency to reduce the frequency of monitoring or to rely on only one test in deciding when to initiate and change therapy. However, when monitoring becomes too infrequent, the effectiveness of the treatment is reduced as patients who have developed resistant strains of the virus go undetected and are treated with inappropriate drugs. Furthermore, there is an efficiency loss to the system as the same drugs could have yielded better results had they been utilized by patients with nonresistant strains of the virus. While the national norms do consider monitoring, the uncertainty that surrounds its marginal utility at different monitoring frequency may partly explain why there is so much variability in its use. In addition, patients who must finance their own care may not see the benefits of an expensive monitoring test as easily as they do the benefits of expensive ARVs. It would be useful to further analyze the present data to document the facility-to-facility variation in monitoring patterns. The INS is also developing a protocol for modeling monitoring under different scenarios to help inform the revision of the national norms.

The study also raises concerns about patients who may be *initiating HAART too late* in the natural history of their HIV disease. Because of the scientific uncertainty regarding when in the process it is clinically beneficial to initiate therapy, optimal use of resources in Mexico almost certainly implies initiating therapy later than in the United States simply because resources are far more constrained in Mexico. However, researchers encountered enormous variability across sites with respect to the initiation of therapy. At one site physicians were so convinced of the benefits of early therapy that they initiated therapy in the absence of CD4 counts (thus even earlier than is the norm in the United States). Other sites, particularly the SSA, which serves the poorest half of the population, had large numbers of patients presenting for HIV diagnosis when they were already severely immunocompromised. The pattern of costs observed showed that the highest costs were incurred in

the year prior to initiating HAART, suggesting that a least an important proportion of patients was initiating treatment in *response* to serious opportunistic illness and not in *anticipation* of when such illness was likely to occur. Depending on the cost of initiating HAART earlier, the cost of treating the initial episode of serious opportunistic illness, and the ability to predict when patients will become symptomatic, earlier HIV detection and initiation of HAART may be not only clinically beneficial but also more efficient.

Finally, while access to ARVs improved dramatically during the period of the study (1997-2001), coverage is far from universal. Patients receiving treatment through the SSA are not guaranteed access to ARVs, while patients in IMSS only have access as long as they are employed. If the patient becomes too sick to work, and as a result loses his or her job, he or she also loses the right to social security. The Ministry of Health's new insurance program for the uninsured currently does not address the need for ARVs. This fragmentation of the public sector is not only an impediment to quality care as patients simultaneously pursue multiple avenues to ensure treatment, it is an inefficient use of resources. Rather than creating parallel diagnostic or treatment capacity to serve the same geographic population, the same resources could be used to extend coverage to those populations whose needs are not being met. Because of the strength of entrenched interests, the government does not currently appear able to address these cross-subsystem inefficiencies (Barraza-Llorens et al. 2002). In contrast, the government is working vigorously to negotiate reductions in the cost of ARVs. It has also recently formed a Mexican Commission on Macroeconomics and Health, which has been tasked to address issues of intellectual property rights and to consider the examples recently set by countries such as Brazil and South Africa that have been more successful in obtaining price reductions for drugs under patent. It should be noted that while the examples of those two countries may be very informative for Mexico because it too has a large domestic market and an active pharmaceutical manufacturing sector, the ability to translate those experiences into lessons for Mexico's small Central American and Caribbean neighbors will be limited.

Annex: Data Behind Graphs

Data for Graphs 1& 2: Distribution of Patients by Type of Therapy

Overall

Calendar year	No Therapy	Mono	Double	Triple	Total
1997	19	2	34	13	68
1998	64	3	64	71	202
1999	216	9	91	226	542
2000	285	6	58	503	852
2001	170	9	50	437	666
Total	***754***	***29***	***297***	***1250***	***2330***

SSA

Calendar year	No Therapy	Mono	Double	Triple	Total
1997	4	0	4	2	10
1998	28	2	9	7	46
1999	139	5	27	77	248
2000	192	4	22	257	475
2001	91	5	13	265	374
Total	***454***	***16***	***75***	***608***	***1153***

IMSS/ISSSTE

Calendar year	No Therapy	Mono	Double	Triple	Total
1997	14	2	28	10	54
1998	28	1	44	46	119
1999	54	2	51	115	222
2000	70	2	28	178	278
2001	59	2	34	131	226
Total	***225***	***9***	***185***	***480***	***899***

INS

Calendar year	No Therapy	Mono	Double	Triple	Total
1997	1	0	2	1	4
1998	8	0	11	18	37
1999	23	2	13	34	72
2000	23	0	8	68	99
2001	20	2	3	41	66
Total	***75***	***4***	***37***	***162***	***278***

Data for Graph 3: Distribution of CD4 Count

Overall

Year	Obs	Mean	Median
-3	17	374	363
-2	68	230	200
-1	319	223	150
1	712	245	180
2	278	313	235
3	140	346	292

SSA

Year	Obs	Mean	Median
-3	5	402	548
-2	35	155	96
-1	206	184	111
1	376	222	155
2	109	281	208
3	40	236	163

IMSS/ISSSTE

Year	Obs	Mean	Median
-3	9	431	451
-2	22	304	286
-1	66	340	255
1	190	290	237
2	110	357	284
3	66	405	355

INS

Year	Obs	Mean	Median
-3	3	155	91
-2	11	323	283
-1	47	233	196
1	146	246	216
2	59	293	237
3	34	361	322

Data for Graphs 4 and 5: Average Annual Per Patient Cost of Treatment by Years, pre- and post-HAART (in US$)

	-3	-2	-1	1	2	3
ARVs	488	360	388	3067	2342	2212
OI Drugs + Procedures	8	26	55	96	54	53
Lab Tests	83	146	341	426	318	354
Outpatient Visits	199	135	145	206	222	291
Hospitalization	45	60	174	124	96	133

Data for Graph 6-9: Average Annual Per Patient Cost of ARV Treatment by Subsystem and by Years pre- and post-HAART (in US$)

SSA

	Average cost of outpatient visits	Average hosp. costs	Average cost OI drugs + procedures	Average cost of non-AIDS specific lab tests	Average cost of AIDS-specific lab tests	Average cost of ARVs	Average total cost
-3	14	26	3	51	31	84	208
-2	17	27	20	98	89	151	402
-1	35	21	55	209	164	177	661
1	71	25	69	245	186	3231	3826
2	57	21	24	196	153	2380	2831
3	65	62	74	422	218	1785	2625

IMSS/ISSSTE

	Average cost of outpatient visits	Average hospitalization costs	Average cost OI drugs + procedures	Average cost of non-AIDS specific lab tests	Average cost of AIDS-specific lab tests	Average cost of ARVs	Average total cost
-3	271	55	4	14	28	610	983
-2	252	103	36	35	30	494	950
-1	321	430	43	135	63	677	1668
1	407	272	86	128	135	2980	4009
2	391	173	67	96	128	2378	3233
3	415	107	38	97	143	2259	3059

INS							
	Average cost of outpatient visits	Average hospitalization costs	Average cost OI drugs + procedures	Average cost of non-AIDS specific lab tests	Average cost of AIDS-specific lab tests	Average cost of ARVs	Average total cost
-3	183	0	87	261	412	996	1940
-2	122	0	7	154	230	762	1275
-1	124	107	96	502	187	537	1552
1	167	89	238	622	268	2652	4036
2	106	43	89	380	166	2123	2905
3	99	334	86	228	200	2601	3549

Data: Unit Cost by Subsystem (in US$)

	SSA	IMSS	ISSSTE	INS
Outpatient visit	8.69	43.63	43.43	19.44
Outpatient visit for drugs	2.65	13.33	13.27	5.94
Hospital day	13.13	191.35	109.62	25.44
Emergency (outpatient)	8.69	52.27	87.46	37.70
Emergency (inpatient)	22.34	269.53	224.89	96.95
Intensive Care Unit day	45.09	1789.50	1013.44	588.42

Data: Total Costs of Drugs by Combination (in US$)

Combination	SSA-C[1]	SSA-G[2]	IMSS	ISSSTE	Cancer	Private
Triple Therapy Regimens						
Indinavir 400mg, Lamivudine 150mg, Zidovudine 250mg (n =)	3293	2852	3167	3207	2161	6425
Indinavir 400mg, Lamivudine 150mg, Zidovudine 100mg (n =)	3314	2871	3188	3216	2391	6467
Didanosine 100mg, Indinavir 400mg, Zidovudine 250 mg (n =)	1670	1447	1607	1606	1096	3259
Estavudine 40mg, Indinavir 400mg, Lamivudine 150mg (n =)	4541	3934	4368	4716	2980	8860
Lamivudine 150mg, Saquinivir 200mg, Zidovudine 250mg (n =)	4660	4037	4483	3858	3059	9093
Lamivudine 150 mg, Nevirapine 200mg, Zidovudine 250mg (n =)	8111	7026	7802	5910	5323	15826

Didanosine 100mg, Indinavir 400mg, Zidovudine 100mg (n =)	1792	1552	1723	1694	1565	3496
Saquinivir 200mg, Zalcitabine .750mg, Zidovudine 100mg (n =)	4829	4183	4645	4163	3385	9422
Estavudine 40mg, Lamivudine 150mg, Nevirapine 200mg (n =)	9359	8107	9003	7419	6142	18261
Abacavir 300mg, Lamivudine 150mg, Zidovudine 250mg (n =)	4794	4153	4612	4583	3147	9355
Dual Therapy Regimens						
Didanosine 100mg, Zidovudine 250mg (n =)	714	619	687	651	469	1394
Didanosine 100mg, Zidovudine 100 mg (n =)	736	637	708	660	699	1436
Lamivudine 150mg, Zidovudine 250 mg (n =)	2337	2024	2248	2252	1534	4560
Indinavir400mg, Lamivudine 150mg/Zidovudine 300mg (n =)	3627	3142	3489	3313	2380	7077
Lamivudine 150mg, Zidovudine 100mg (n =)	2358	2043	2268	2261	1764	4601

[1]SSA Cuernavaca
[2]SSA Guadalajara

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