An Approach to Evaluating HAART Utilization and Outcomes in CARE Act-Funded Clinics

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The following reports address program evaluation-related issues relevant to the CARE Act community. To obtain copies, visit the HRSA HIV/AIDS Bureau web site at http://www.hrsa.gov/hab/ evaluation.html or contact the HRSA Information Center at 1-888-ASK-HRSA (1-888-275-4772).

Choosing and Using an External Evaluator, Report #1, September 1997. This guide offers advice on the effective selection and use of external evaluators. It describes a seven-step process for defining the purpose and scope of an evaluation, identifying the evaluator's tasks, soliciting and selecting the evaluator, and working with the evaluator to plan and implement a methodologically sound study.

Using Data to Assess HIV/AIDS Service Needs: A Guide for Ryan White CARE Act Planning Groups, Report #2, August 1998. This guide provides materials for orienting and training members of CARE Act planning groups to read statistical reports, conduct or oversee community needs assessments, and use epidemiologic and administrative data for HIV service planning and decision making.

Cost- and Performance-Based Contracting: A Guide for Ryan White CARE Act Grantees, Report #3, October 1998. This guide defines cost and outcome effectiveness and discusses the ways in which cost and performance indicators can be incorporated into CARE Act priority-setting, resource allocation, and procurement processes. Service procurement models that link reimbursement to the accomplishment of performance targets are discussed, along with strategies for preventing and solving performance problems.

A Practical Guide to Evaluation and Evaluation Terms for Ryan White CARE Act Grantees, Report #4, September 1999. This guide is designed to help CARE Act grantees and planning groups become familiar with the "language" of evaluation. Part 1 defines evaluation and explains how evaluation differs from needs assessment, monitoring, research, and continuous quality improvement. Part 2 describes the steps involved in designing and conducting evaluations and defines the terms associated with each step. Part 3 defines terms related to quality management and improvement.

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Preface

This guide is one of a series of publications that are being developed by the Health Resources and Services Administration's (HRSA), HIV/AIDS Bureau (HAB) to assist Ryan White Comprehensive AIDS Resources Emergency (CARE) Act grantees in designing and implementing evaluation studies. The reports provide guidance on a wide range of evaluation issues and describe evaluation studies conducted by CARE Act grantees. The goal of the series is to improve services for people living with HIV/AIDS by enhancing the ability of CARE Act grantees to conduct methodologically sound evaluations and to develop action plans based on study findings.

An Evaluation Monograph Advisory Committee, consisting of one representative from each CARE Act Title, provides guidance and oversight for the series. Committee members advise HAB staff on evaluation topics that should be addressed and the criteria that should be used to select publications. They also review draft reports to suggest ways of making the information more useful and understandable to grantees. Committee members include:

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This report is based on a Master's thesis, entitled *Clinical Outcomes and Utilization of Health Care Services in Two HIV-Infected Populations,* which was prepared by Dorothy L. Keininger, Department of Pharmacy Practice and Science, University of Arizona. Ms. Keininger now serves as Director, Research and Education Department for the MAPI Research Institute in Lyon, France.

Notes:

Executive Summary

This report describes a relatively low-cost method of evaluating the outcomes of HIV-related primary medical care. Adapted from a Master's thesis, the report details the approach used by two Title III-funded clinics to evaluate the therapeutic benefits and resource requirements of implementing highly active antiretroviral therapy (HAART). Study findings are presented, but the primary focus of the report is on the *process* of designing and conducting an outcomes evaluation, the problems encountered, and the "lessons learned."

In January 1998, Maricopa Integrated Health System (MIHS) contracted with the University of Arizona to conduct a comparative study of HAART utilization and outcomes in two HIV clinics—McDowell Healthcare Center, a Phoenix-based clinic operated by MIHS, and El Rio Special Immunology Associates, a Tucson-based clinic operated by the El Rio Santa Cruz Neighborhood Health Center. This report describes the rationale for the study, the evaluation design, implementation steps, results, limitations of the study, dissemination and use of the evaluation findings, and lessons learned. The sections are organized as follows:

Background

This section describes the three classes of antiretroviral drugs used in combination therapies and the rationale for conducting a comparative study.

Designing the Evaluation

This section describes the evaluation objectives, the study design (a retrospective cohort analysis), the sample selection process, the independent and dependent variables studied, and the indicators used to measure each dependent variable. The development of a medical record abstraction tool to collect core data elements also is discussed.

Implementing the Evaluation

This section summarizes the data collection process, including the training of certified medical records technicians to abstract data from medical records, quality control procedures, and procedures for protecting patient confidentiality.

Results

Contrary to expectations, the mean viral loads per patient were similar for patients on triple therapy (i.e., at least three antiretroviral drugs including a protease inhibitor) and patients not on triple therapy. However, the triple therapy group had a significantly lower mortality rate. The triple therapy group averaged more physician visits, viral load tests, and $CD4^+$ laboratory tests per patient but did not have significantly lower mean values for emergency room visits per patient or hospital admissions per patient.

Limitations of the Study

This section describes several aspects of the study's design, implementation, and analysis that limit the conclusions that can be drawn. Patient and clinic characteristics that may have influenced therapeutic outcomes and resource utilization are discussed, along with the need for a broader definition of triple therapy.

Dissemination and Use of Evaluation Findings

This section describes how Maricopa Integrated Health System has used evaluation findings to improve McDowell Healthcare Center's clinical database, analyze resource use and cost by disease stage, and design a follow-up study on HAART adherence.

Lessons Learned

This section presents an itemized budget for the evaluation and summarizes what was learned about time requirements, essential skills, and contractual arrangements. A major lesson learned was to keep the evaluation focused on a few key objectives that can be accomplished within the allotted budget and timeframe.

Introduction

In January 1998, Maricopa Integrated Health System (Phoenix, Arizona) contracted with the University of Arizona to conduct an evaluation of highly active antiretroviral therapy (HAART) utilization and outcomes in two HIV clinics funded by Title III of the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act. With financial support from a Title III supplemental grant, this study sought to compare HAART prescribing patterns, therapeutic outcomes, and health care resource utilization at McDowell Healthcare Center (McDowell), a Phoenix-based HIV clinic operated by Maricopa Integrated Health System, and El Rio Special Immunology Associates (El Rio), a Tucson-based HIV clinic operated by the El Rio Santa Cruz Neighborhood Health Center. Because these clinics primarily served low-income patients who were similarly distributed by age, gender, and mode of exposure, they served as useful comparison sites for assessing trends in HAART prescribing patterns and the therapeutic benefits of initiating HAART at different levels of disease severity.

The Arizona study offers an example of a relatively low-cost approach to outcomes evaluation.[1] The study also highlights some of the "real-world" problems that evaluators encounter when they attempt to measure program outcomes. This report summarizes the study's methodology and findings, with particular emphasis on the "lessons learned."

The report has four purposes:

- *To describe the process of designing, conducting, and analyzing an outcomes evaluation;*
- *To provide examples of key outcomes indicators and data elements;*
- *To present the study's major findings; and*
- *To describe the ways in which study findings are being used for program enhancement and improvement.*

[1] See "Lessons Learned" for itemized budget.

The contents of this report are based on a Master's thesis, entitled *Clinical Outcomes and Utilization of Health Care Services in Two HIV-Infected Populations,* which was prepared by Dorothy L. Keininger, Department of Pharmacy Practice and Science, University of Arizona. With the permission of Maricopa Integrated Health System and Ms. Keininger, the report was adapted to emphasize the evaluation methodology and to simplify statistical discussions of evaluation results. Readers seeking more detailed descriptions of the study data and the results of statistical tests should consult the tables in the appendix. Study limitations are discussed on pages 20-21.

Key Terms

Deoxyribonucleic acid (DNA) is the molecule that encodes genetic information.

Highly active antiretroviral therapy (HAART) refers to any antiretroviral regimen that can be expected to reduce viral load to less than 50 copies per milliliter in patients who have not previously received antiretroviral therapy.

Nucleoside analogue reverse transcriptase inhibitors (NRTIs) are antiretroviral drugs that attack HIV at an early stage of the viral replication process. These drugs inhibit the action of reverse transcriptase, the enzyme that allows HIV to change its genetic material into a form that can enter the infected cell's nucleus.

Nonnucleoside reverse transcriptase inhibitors (NNRTIs) are antiretroviral drugs that attack HIV by binding directly onto reverse transcriptase and preventing the conversion of RNA to DNA.

Protease inhibitors are antiretroviral drugs that block the action of the HIV protease enzyme, thereby preventing HIV replication. Unlike reverse transcriptase inhibitors, protease inhibitors can inhibit HIV replication in cells that already are infected.

Ribonucleic acid (RNA) is a chemical found in the nucleus and cytoplasm of cells. It plays an important role in protein synthesis and other chemical activities of the cell.

Triple therapy was defined in this study as a regimen of at least three antiretroviral drugs, including at least one protease inhibitor. Based on the success of NRTI/NNRTI combinations in recent clinical trials, many clinicians now define triple therapy as a regimen of at least three antiretroviral drugs, with one being a protease inhibitor or an NNRTI (particularly efavirenz).

Viral load is the amount of virus in the blood or other tissues. The presence of HIV RNA indicates that the virus is replicating. Changes in viral load are used to gauge drug effectiveness and disease progression.

Background

Over the past 13 years, the United States has witnessed major advances in the medical treatment of HIV infection. **These advances include:**

- *An improved understanding of all stages of viral replication;*
- *The development of viral load tests to measure the amount of plasma HIV RNA (HIV virus) in the blood;*
- *The increased use of prophylactic drugs to prevent opportunistic infections; and*
- *The development and testing of new combinations of antiretroviral drugs that suppress HIV replication.*

Three classes of antiretroviral drugs are used in combination therapies. Between 1987 and 1995, the U.S. Food and Drug Administration (FDA) approved five nucleoside analogue reverse transcriptase inhibitors (NRTIs)—zidovudine (ZDV), didanosine (ddI), zalcitabine (ddC), stavudine (d4T), and lamivudine (3TC)—for HIV treatment. These drugs attack HIV at an early stage of the viral replication process by inhibiting the action of reverse transcriptase, the enzyme that allows HIV to change its genetic material into a form that can enter the infected cell's nucleus.

In 1996 and 1997, the first nonnucleoside reverse transcriptase inhibitors (NNRTIs) became available. NNRTIs, such as nevirapine and delavirdine, also work at an early stage of the viral replication process by binding directly onto reverse transcriptase and preventing the conversion of ribonucleic acid (RNA) to deoxyribonucleic acid (DNA).

Between 1995 and 1997, the FDA approved four protease inhibitors—saquinavir, ritonavir, indinavir, and nelfinavir—for HIV treatment. In contrast to NRTIs and NNRTIs, protease inhibitors attack HIV at the last stage of the viral replication process. When HIV enters a cell's nucleus, it prepares to replicate by making long chains of structural proteins and enzymes. Protease inhibitors prevent the protease enzyme from cutting these chains into the

shorter pieces needed to form new copies of HIV. Although some replication still occurs, the new copies are more likely to be defective and, therefore, incapable of infecting other cells. When a protease inhibitor is combined with two NRTIs in a "triple therapy" regimen, many patients experience dramatic and sustained reductions in viral load.

To decide which combinations of antiretroviral drugs are likely to work best for their patients, medical professionals rely upon clinical trials and expert opinion. Clinical trials provide a strong scientific approach for determining whether one drug combination is more effective than another. By ensuring that patients meet specific eligibility criteria and then randomly assigning them to an *intervention* (new treatment) or *control* (standard treatment) group, researchers are able to limit the factors that could bias study findings. However, clinical trials have an important limitation. Because these studies are conducted with select groups of patients under highly controlled conditions, the results may not be generalizable to populations, geographic areas, or health care settings that differ from those in the clinical trial.

In Arizona, low-income residents with HIV/AIDS typically obtain antiretroviral drugs through a Medicaid alternative program—the Arizona Health Care Cost Containment System (AHCCCS)—or the State AIDS Drug Assistance Program (ADAP). While waiting for protease inhibitors to be added to the AHCCCS and ADAP formularies, El Rio and McDowell physicians obtained these drugs for many patients through local clinical trials. They had noted health improvements for some patients, but their anecdotal sense was that the therapeutic outcomes were not as significant as those presented in the scientific literature. Discussions between El Rio's medical director and a graduate research associate in the University of Arizona's Department of Pharmacy Practice and Science led to the idea of evaluating the effectiveness of HAART through a comparative study of prescribing patterns and therapeutic outcomes at the two clinics. Working with the grant administrator at Maricopa Integrated Health System, the graduate research associate developed a proposal for Title III supplemental funding.

Designing the Evaluation[2]

Representatives of Maricopa Integrated Health System, the University of Arizona, and the two clinics **established six objectives for the evaluation:**

1) To compare triple therapy prescribing trends at the two clinics;

2) To determine whether the clinics were initiating triple therapy at different levels of disease severity;

3) To compare patients' therapeutic outcomes by clinic;

4) To compare patients' therapeutic outcomes by treatment type (triple therapy vs. non-triple therapy);

5) To compare patients' utilization of health care resources by clinic; and

6) To compare patients' utilization of health care resources by treatment type (triple therapy vs. non-triple therapy).

The graduate research associate from the University of Arizona's Department of Pharmacy Practice and Science served as principal investigator for the evaluation. A thesis committee, consisting of the grant administrator from Maricopa Integrated Health System and faculty from the University of Arizona's College of Pharmacy, reviewed the proposed study design and provided ongoing advice and guidance.

Study Design

The study team (principal investigator and thesis committee) chose January 1, 1996 through October 31, 1997 as the study period. They expected clinic differences in prescribing patterns to be most pronounced during this period because protease inhibitors were still very new and HIV specialists had not reached consensus on the most appropriate disease stage at which to initiate triple therapy. Since the study period had already passed, they designed the

2 For more detailed definitions and examples of the evaluation terms used in this section, see *A Practical Guide to Evaluation and Evaluation Terms for Ryan White CARE Act Grantees* (Report #4) in the HIV/AIDS Bureau's Evaluation Monograph Series. This guide can be accessed at http://www.hrsa.gov/hab/evaluation.html.

study as a retrospective cohort analysis. This strategy involved collecting data from outpatient medical records for a random sample of patients treated at each clinic between January 1996 and October 1997. Random sampling was used to ensure that study participants would be representative of El Rio and McDowell patients.

Sample Selection

El Rio and McDowell were selected as the study sites based on two criteria: (1) their mutual interest in evaluating the therapeutic benefits of HAART for uninsured and socioeconomically disadvantaged patients and (2) anecdotal evidence that they had implemented protease inhibitor-based therapy at different rates. Because these clinics were well matched in terms of service offerings and patient characteristics, the study team hoped to minimize the influence of "confounding factors" when analyzing differences between clinics and treatment types. However, they recognized that, with only two study sites, their findings could not be generalized beyond these settings. (See "Limitations of the Study.")

McDowell Healthcare Center

Since its founding in 1989, McDowell had grown to be the largest provider of HIV-related medical care in Maricopa County. Staffed by an integrated team of medical, mental health, and social service professionals, this clinic offered HIV counseling and testing, outpatient primary medical care, dental care, and behavioral health services. Through a collaborative arrangement with Phoenix Body Positive, a nonprofit AIDS service organization, McDowell also enrolled patients in community-based pharmaceutical clinical trials. During the study period, privately insured individuals and Medicare beneficiaries accounted for less than 15 percent of McDowell's patients. Of the remaining patients, 40 percent were covered by an AHCCCS plan, and 60 percent qualified for CARE Act support because they were uninsured.

El Rio Special Immunology Associates

El Rio had been serving HIV-positive patients in the Tucson area since 1992. Staffed by physicians, nurses, a nutritionist, and mental health professionals, this clinic provided outpatient primary medical care, diagnostic laboratory and radiology testing, nutritional counseling, and behavioral health services. As a clinical trials site for the Arizona Clinical Research Corporation, El Rio also enrolled patients in pharmaceutical clinical trials. During the study period, privately insured individuals and Medicare beneficiaries accounted for less than 15 percent of El Rio's patients. Coverage for the remaining patients was about evenly split between AHCCCS and the CARE Act.

Participant Selection

The study team began the participant selection process by determining the size of each clinic's eligible population. **To be included in the study, patients had to meet four criteria:**

1) Clinically documented as HIV-positive;

2) Received medical care at one of the clinics as of January 1, 1996;

3) Care funded by AHCCCS or the CARE Act; and

4) Received medical care for at least six months during the study period.

Privately insured patients and Medicare beneficiaries were excluded from the selection process to focus the study on uninsured and socioeconomically disadvantaged patients.

All eligible El Rio patients (N=237) were included in the study. The McDowell sample was randomly selected from 750 patients who met the inclusion criteria. After estimating the sample size necessary to be representative of McDowell's eligible patients, the study team randomly chose a number between 1 and 10 for use in selecting study participants. Since this number was three, they began with the third patient on the eligible list and chose every third patient thereafter. This process resulted in the selection of 254 McDowell patients.

Variables and Measures

In evaluation studies, *variables* are the observable characteristics that evaluators count or measure. *Independent variables* are the presumed causes of some change. *Dependent variables* are the health behaviors or health indicators that are expected to change.

This study examined two independent variables: (1) clinic providing treatment (El Rio or McDowell) and (2) treatment type (triple therapy or non-triple therapy). **The clinics were compared with respect to four dependent variables:**

1) Proportion of patients receiving triple therapy;

2) Patients' disease severity at initiation of triple therapy;

3) Patients' therapeutic outcomes; and

4) Patients' utilization of health care resources.

Patients receiving each treatment type were compared with respect to therapeutic outcomes and health care resource utilization. The triple therapy group included patients who were treated with at least one protease inhibitor and two additional antiretroviral drugs for any period of time. The non-triple therapy group included all other patients.

Table 1 shows the indicators used to measure each variable. The term "mean" refers to the average value for a particular measure. To calculate mean $CD4^+$ lymphocyte count at initiation of triple therapy, the study team used each patient's recorded count at the date closest to initiation of triple therapy. After adding these individual $CD4^+$ lymphocyte counts, they divided the sum by the total number of patients on triple therapy to derive the mean. The same process was used to calculate mean viral load at initiation of triple therapy.

Table 1. Indicators Used to Measure Dependent Variables

Dependent Variable	Measures
Proportion of Patients Receiving Triple Therapy	% of patients receiving triple therapy % of patients not receiving triple therapy
Disease Severity at Initiation of Triple Therapy*	% of patients who were asymptomatic/ symptomatic vs. AIDS-defined Mean viral load Mean $CD4^+$ lymphocyte count
Therapeutic Outcomes	Mean viral load per patient Mean $CD4^+$ lymphocyte count per patient Mean number of AIDS-defining opportunistic infections per patient Mortality rate (% of patients who died)
Utilization of Health Care Resources	Mean number of HIV-related outpatient physician visits per patient Mean number of $CD4^+$ laboratory tests per patient Mean number of viral load tests per patient Mean number of HIV-related hospital admissions per patient Mean number of HIV-related emergency room visits per patient

* The CDC 1993 revised HIV classification system was used to categorize disease severity.

The calculation of mean $CD4^+$ lymphocyte count per patient during the total study period involved a two-step process. First, each patient's mean $CD4^+$ lymphocyte count was calculated by adding all of her/his recorded counts and dividing by the total number of times that $CD4^+$ laboratory tests were administered. Second, the study team added the mean counts for individual patients and divided the sum by the total number of patients. The same process was used to calculate mean viral load per patient, mean number of AIDS-defining opportunistic infections per patient, and mean utilization of health care resources per patient.

Development of Medical Record Abstraction Tool

A subcontractor worked with the principal investigator and her faculty advisor to develop a Microsoft Access™ spreadsheet that would allow data from medical records to be entered directly onto laptop computers. This electronic spreadsheet was designed to collect the following core data elements:

Patient Demographics	Clinic/Treatment Data	Therapeutic Outcomes	Resource Utilization
• Patient identification number	• Name of clinic providing treatment	• Plasma HIV RNA levels (i.e., viral loads)	• HIV-related outpatient physician visits
• Gender	• Antiretroviral regimen over the study period	• $CD4^+$ lymphocyte counts	• HIV-related laboratory tests (i.e., $CD4^+$ laboratory tests; viral load tests)
• Race/ethnicity		• AIDS-defining opportunistic infections	• HIV-related emergency room visits
• Mode of exposure		• Mortality	• HIV-related hospital admissions
• Comorbidities (i.e., intravenous drug use; chronic mental illness)			

In addition to storing data, the spreadsheet program was able to perform edit checks. For example, if a medical record abstracter entered a $CD4^+$ lymphocyte count that did not fall within a specified range, the program would flag this entry for review.

Implementing the Evaluation

Maricopa Integrated Health System contracted with two certified medical records technicians (MRTs) to collect data from outpatient medical records. Because the medical records were not computerized and the MRTs worked only part time, the medical record abstraction process took three months. Each medical record took 45-60 minutes to abstract.

Training and Quality Control Procedures

After pilot-testing the medical record abstraction tool, the principal investigator conducted a one-day training session for the MRTs and conducted on-site visits to observe data collection. To assess the accuracy of the abstracted data, the principal investigator rechecked a 10 percent random sample of patient records. She discovered that, during part of the study period, the MRTs had mistakenly recorded branched-chain DNA (bDNA) test values as reverse transcriptase polymerase chain reaction (RT-PCR) test values. She also discovered that the MRTs were not recording data on patients who had died or who had made only a couple of physician visits. These errors were corrected prior to data analysis.

Key Terms

Branched-chain DNA (bDNA) test directly measures the amount of plasma HIV RNA in the blood (i.e., viral load) by setting off a chemical reaction so that the HIV RNA emits light. The amount of light indicates the level of RNA in the sample.

Human subjects committee (also called institutional review board) is a committee in a hospital, university, or other institution that provides peer review for proposed research studies and evaluation studies that collect data on human subjects for research purposes.

Reverse transcriptase polymerase chain reaction (RT-PCR) test measures the amount of plasma HIV RNA indirectly. This test chemically multiplies viral RNA that exists in the sample by a factor of approximately one million. The amount of RNA then must be calculated. Because the bDNA and RT-PCR test methods differ, one type of test must be used consistently to assess viral load trends.

Procedures for Protecting Patient Confidentiality

The MRTs signed confidentiality agreements, promising not to disclose any information on individual patients. Data from medical records were transferred directly to the electronic spreadsheet. Although these data included each patient's nine-digit medical record number, the charts could not be located without knowing the specific filing algorithms used by the clinics. To further protect patient confidentiality, the computer software generated new patient identification numbers for use in data analysis.

Because the study team planned to collect data on human subjects for research purposes, they submitted a "Request for Ethical Review" to human subjects committees at the University of Arizona Health Sciences Center and Maricopa Integrated Health System. This document briefly described the study's purpose and background; target population; methodology; procedures for maintaining data confidentiality; and the benefits, costs, and risks to study participants. Due to the retrospective nature of the research and the provisions for patient confidentiality, both committees exempted the study from further review.

Results

This section provides an overview of the evaluation's major findings. Descriptive data on the study samples and the results of statistical tests are presented in the appendix (Tables 2-21). When comparing clinics or treatment types, the study team looked for "statistically significant" differences. Tests of statistical significance assess whether an observed difference is larger or smaller than would be expected by chance alone. In this study, differences were regarded as statistically significant if there was a five percent or less probability ($p \leq 0.05$) that they could have occurred by chance alone.

Patient Demographics by Clinic

The patients selected for medical record review at the two clinics were fairly well matched in terms of age, gender, race/ethnicity, and mode of exposure (Table 2). At El Rio, patient ages ranged from 15 to 58 years (mean = 36 years). At McDowell, patient ages ranged from 19 to 63 years (mean = 35 years). Men accounted for more than 80 percent of both samples. The majority of patients in each sample were non-Hispanic whites (60% at El Rio; 66% at McDowell). However, Hispanic patients accounted for a much higher proportion of the El Rio sample (32% vs. 20%). At both clinics, more than half of the patients reported male-to-male sexual contact as the mode of HIV exposure. El Rio had a higher proportion of patients who acquired HIV through intravenous drug use (23% vs. 11%). McDowell had a higher proportion of patients who acquired HIV through heterosexual contact with an infected partner (17% vs. 7%).

At the beginning of the study period, the clinics had similar proportions of patients with comorbidities (Table 3). Almost 90 percent of the patients in each sample had never experienced an AIDS-defining opportunistic infection. However, when both $CD4^+$ lymphocyte counts and opportunistic infections were considered, the proportion of AIDS-defined patients at El Rio (27%) was significantly higher than the proportion at McDowell (19%).

Inter-clinic comparisons revealed significant differences in the proportion of patients who could not be tracked over the entire study period because they died, moved, entered a nursing home, experienced a change in insurance status, or stopped receiving care for unknown reasons (Table 3). Thirty-six percent of McDowell patients were "lost to follow-up," as compared to only 23 percent of El Rio patients. More than half of the patients who stopped receiving care at McDowell were "lost to follow-up" for unknown or unreported reasons.

To assess whether evaluation results might be biased by McDowell's high dropout rate, the study team looked for possible differences between the patients remaining in each clinic's sample. They found one reason to suspect that the patients remaining in McDowell's sample might have been healthier than their El Rio counterparts. During the study period, McDowell was one of many CARE Act and AHCCCS providers in Maricopa County. When McDowell's uninsured patients were admitted to the hospital, the State Medicaid Program auto-assigned them to one of nine AHCCCS plans. Because McDowell participated in only one AHCCCS plan, very few patients returned to this clinic after hospitalization. El Rio, on the other hand, was a contracted provider for all AHCCCS plans in Pima County. Uninsured patients who became eligible for AHCCCS during hospitalization usually returned to El Rio after discharge.

Patient Demographics by Treatment Type

Patients in the triple therapy and non-triple therapy groups were similarly distributed with respect to age, gender, race/ethnicity, and mode of exposure (Table 4). Ages in the triple therapy group ranged from 16 to 58 years (mean = 36 years). Ages in the non-triple therapy group ranged from 19 to 63 years (mean = 35 years). Men accounted for 86 percent of both treatment groups. Although two-thirds of the patients in each treatment group were non-Hispanic whites, the triple therapy group had a higher proportion of Hispanic patients (30% vs. 22%). More than half of the patients in each group had acquired HIV through male-to-male sexual contact. The non-triple therapy group had a slightly higher percentage of patients with intravenous drug use as the mode of exposure (19% vs. 15%). About 12 percent of the patients in both groups had acquired HIV through heterosexual contact.

At the beginning of the study period, the treatment groups had similar proportions of patients with comorbidities and AIDS-defining opportunistic infections (Table 5). However, when both $CD4^+$ lymphocyte counts and opportunistic infections were considered, the triple therapy group had a significantly higher proportion of AIDS-defined patients (29% vs. 15%). Seventy percent of the patients diagnosed with AIDS at baseline (January 1, 1996) received triple therapy at some time during the study period. Because clinic physicians did not routinely document patient refusals or the reasons for treatment failures, the study team was unable to determine why 30 percent of AIDS-defined patients did not receive triple therapy.

The non-triple therapy group had a significantly higher proportion of patients who could not be tracked over the entire study period (44% vs. 18%). In both groups, almost half of the patients who stopped receiving care were "lost to follow-up" for unknown or unreported reasons. The high dropout rate in the non-triple therapy group may have biased statistical analyses of relationships between therapeutic outcomes and treatment type.

Triple Therapy Prescribing Trends

The first study objective was to compare triple therapy prescribing trends at the two clinics. Over the study period, a significantly higher proportion of patients received triple therapy at El Rio than at McDowell (Table 6). Sixty-three percent of El Rio patients received triple therapy, as compared to 47 percent of McDowell patients.

Changes in the proportion of patients receiving triple therapy at each clinic were recorded at three-month intervals (Table 7). Although both clinics dramatically increased their use of triple therapy over the study period, they initiated triple therapy at different rates. El Rio physicians began prescribing triple therapy soon after protease inhibitors became available. By the first quarter of 1997, almost half of their patients were receiving triple therapy. The proportion of El Rio patients on triple therapy continued to increase, reaching a high of 71 percent during the third quarter of 1997.

McDowell physicians placed very few patients on triple therapy during 1996. By the first quarter of 1997, only 24 percent of their patients were receiving triple therapy. Between the second and third quarters of 1997, the proportion of patients on triple therapy jumped from 36 percent to 60 percent.

Disease Severity at Initiation of Triple Therapy

The second study objective was to determine whether El Rio and McDowell initiated triple therapy at different levels of disease severity. If one clinic initiated triple therapy earlier in the disease process than the other, the therapeutic outcomes of these different prescribing patterns could be compared. **Disease severity at initiation of triple therapy was examined using three measures:**

1) Asymptomatic/symptomatic vs. AIDS-defined;

2) Mean viral load; and

3) Mean CD4⁺ lymphocyte count.

Disease Stage

An analysis of the patients at each clinic who received triple therapy revealed significant differences in prescribing patterns based on disease stage (Table 8). El Rio physicians tended to initiate triple therapy at earlier stages of disease. Half of El Rio's triple-therapy patients were asymptomatic or symptomatic when triple therapy was initiated, as compared to only 37 percent of McDowell's triple-therapy patients.

Another analysis compared the proportions of asymptomatic/symptomatic patients that received triple therapy at each clinic (Table 9). The proportion of asymptomatic/symptomatic patients receiving triple therapy at El Rio (56%) was significantly higher than the proportion receiving triple therapy at McDowell (31%). However, the clinics placed similar proportions of AIDS-defined patients on triple therapy (72% at El Rio and 68% at McDowell). (See Table 10.)

Clinical Indicators

Viral load and CD4⁺ lymphocyte count were used as additional measures of disease severity at initiation of triple therapy. Viral load refers to the quantity of plasma HIV RNA that is in the blood. Because research studies have shown viral load to be a strong predictor of disease progression, physicians use baseline viral load to determine when to start antiretroviral therapy. CD4⁺ lymphocyte counts provide information about the status of the immune system. In contrast to viral load testing which indicates how quickly the virus is multiplying, CD4⁺ lymphocyte tests measure the damage that the

immune system has sustained. By monitoring both $CD4^+$ level and viral load, physicians are able to obtain a more complete picture of immune health.

A comparison of patients on triple therapy at each clinic revealed that El Rio patients had a significantly lower mean viral load at initiation of triple therapy (Table 11). This finding provided additional evidence that El Rio physicians were prescribing triple therapy at earlier stages of disease. Although El Rio patients had a higher mean $CD4^+$ lymphocyte count at initiation of triple therapy, the difference between clinics was not significant.

Therapeutic Outcomes by Clinic

The third study objective was to compare patients' therapeutic outcomes by clinic. The study team compared outcomes for the total study period and at three-month intervals. Their measures included mean viral load per patient, mean $CD4^+$ lymphocyte count per patient, mean number of AIDS-defining opportunistic infections per patient, and mortality rate.

Total Study Period

No significant inter-clinic differences were found in mean viral load per patient, $CD4^+$ lymphocyte count per patient, or the mean number of AIDS-defining opportunistic infections per patient (Table 12). Given that a much higher proportion of El Rio patients received triple therapy over the study period (63% vs. 47%), these findings were unexpected. Informal discussions revealed that McDowell physicians had placed many patients on "protease-sparing" NRTI/NNRTI combinations during the study period.[3] Because these antiretroviral regimens did not include a protease inhibitor, they did not meet the study's definition of triple therapy. However, they may have been as effective as NRTI/protease inhibitor combinations in suppressing viral replication and preserving immune function. (See "Limitations of the Study" for other factors that may have influenced therapeutic outcomes.)

The mortality rate for each clinic was calculated by dividing the number of clients who died by the total number of clients in the sample (Table 13). Although El Rio had a higher mortality rate (8% vs. 4%), the high proportions of patients "lost to follow-up" may have biased this analysis. Because the vital status of these patients could not be tracked, the "true" number of

[3] The most common protease-sparing regimens were as follows: (1) ZDV, 3TC, and nevirapine; (2) 3TC, d4T, and nevirapine; and (3) ddI, d4T, and nevirapine.

deaths at each clinic could not be determined. Also, the higher proportion of patients "lost to follow-up" at McDowell (36% vs. 23%) may have resulted in self-selection of a healthier sample.

Quarterly Trends

To identify trends in therapeutic outcomes, the study team analyzed quarterly changes in each clinic's mean viral load per patient, mean $CD4^+$ lymphocyte count per patient, mean number of AIDS-defining opportunistic infections per patient, and mortality rates. Therapeutic outcomes improved for both clinics as they increasingly prescribed triple therapy.

In all but one quarter, both clinics experienced a steady decline in mean viral load per patient (Table 14). Although El Rio had much higher proportions of patients on triple therapy throughout the study period, El Rio's mean viral load per patient was significantly lower than McDowell's only in the fourth quarter of 1996. At that time, 38 percent of El Rio patients were receiving triple therapy, as compared to 13 percent of McDowell patients.

During 1996, neither clinic experienced a consistent trend in mean $CD4^+$ lymphocyte count per patient (Table 15). Mean values at each clinic steadily increased during 1997, but no significant inter-clinic differences were noted.

Over the study period, both clinics experienced declines in the mean number of AIDS-defining opportunistic infections per patient (Table 16) and mortality rates (Table 17). Inter-clinic differences were not significant in any quarter.

Therapeutic Outcomes by Treatment Type

The fourth study objective was to compare patients' therapeutic outcomes by treatment type (triple therapy vs. non-triple therapy). The outcomes measures included mean viral load per patient, mean $CD4^+$ lymphocyte count per patient, and mean number of AIDS-defining opportunistic infections per patient (Table 18). Contrary to expectations, the groups had similar mean viral loads per patient. The triple therapy group had a significantly *lower* mean $CD4^+$ lymphocyte count per patient and a significantly *higher* mean number of opportunistic infections per patient. However, when opportunistic infections that preceded the initiation of triple therapy were excluded from the analysis, the triple therapy group had a slightly lower mean number of opportunistic infections per patient.

To further evaluate therapeutic outcomes by treatment type, the study team compared mortality rates (Table 19). Consistent with the findings of clinical trials, the triple therapy group had a significantly lower mortality rate (3% vs. 10%).

Utilization of Health Care Resources by Clinic

During the study period, the annual cost of prescribing triple therapy for one patient was estimated to be more than $10,000. Recognizing that pharmaceutical costs and associated physician visits and laboratory tests could be partially offset by reduced emergency room visits and hospitalizations, the study team decided to evaluate use of both outpatient and inpatient resources.

A comparison of the two clinics revealed that El Rio patients used more of every resource during the study period (Table 20). Because a higher proportion of El Rio patients received triple therapy, the study team expected the mean number of physician visits, viral load tests, and $CD4^+$ laboratory tests per patient to be significantly higher at this clinic. Frequent monitoring is necessary to evaluate treatment response, adverse effects, and adherence. Contrary to expectations, El Rio's mean number of emergency room visits per patient and mean number of hospital admissions per patient also were significantly higher. This analysis may have been biased by McDowell's inability to document emergency room visits and hospital admissions for patients assigned to another AHCCCS plan during hospitalization. (See "Patient Demographics by Clinic.")

Utilization of Health Care Resources by Treatment Type

Using the same measures, the study team compared health care resource utilization by patients receiving each treatment type (Table 21). As expected, the triple therapy group averaged more physician visits, viral load tests, and $CD4^+$ laboratory tests per patient. However, the triple therapy group did not have significantly lower mean values for emergency room visits per patient or hospital admissions per patient. The lack of significant differences may have been due to the therapeutic effectiveness of McDowell's protease-sparing therapies and/or incomplete data on McDowell patients who were assigned to another AHCCCS plan during hospitalization. (See "Patient Demographics by Clinic" and "Therapeutic Outcomes by Clinic.")

Limitations of the Study

Several aspects of this study's design, implementation, and analysis limit the conclusions that can be drawn.

1) **The study design considered only two treatment types—triple therapy and non-triple therapy.** Because antiretroviral regimens had to include at least one protease inhibitor to meet the study's definition of triple therapy, the protease-sparing regimens prescribed by McDowell physicians were classified as non-triple therapy. As previously discussed, this classification scheme may have confounded the study results.

2) **Some of the data needed for comparisons of clinics and treatment types were not uniformly available.** For example, the study team had planned to use HIV-related conditions, such as persistent fever, diarrhea, and weight loss, to distinguish between asymptomatic and symptomatic patients at baseline. Because clinic physicians did not routinely document these conditions, asymptomatic and symptomatic patients had to be grouped together for analytical purposes. McDowell's inability to track patients assigned to other AHCCCS plans during hospitalization further complicated comparisons of clinics and treatment types.

3) **When analyzing differences between clinics or treatment types, the study team did not control for patient or clinic characteristics that might have influenced therapeutic outcomes and health care resource utilization.**[4] Relationships between treatment type and therapeutic outcomes might have been influenced by patient characteristics, such as disease severity, length of time on triple therapy, comorbidities, extent of adherence to the drug regimen, and/or development of viral resistance. Relationships between clinic setting and therapeutic outcomes might have been influenced by these patient characteristics, as well as differences in the proportion of patients receiving prophylaxis for opportunistic infections. The different proportions of patients "lost to follow-up" at each clinic also might have influenced therapeutic outcomes. Multivariate models

[4] Some of these data were not available in medical records.

that adjusted for these variables would have provided a more comprehensive explanation of observed variability in therapeutic outcomes and resource use.

4) **When calculating mean values for therapeutic outcomes and resource utilization, the study team included measures taken before and after the initiation of triple therapy.** If a large number of patients had very low $CD4^+$ lymphocyte counts, high viral loads, and/or high resource utilization before starting triple therapy, the inclusion of these "pre-triple-therapy" values would obscure the true effect of triple therapy.

5) **Because this evaluation involved only two clinics that were not randomly selected, the findings cannot be generalized beyond these two settings.** However, both clinics found the study to be very helpful in documenting the therapeutic outcomes and resource use associated with their prescribing patterns. Remaining sections of this report describe the ways in which Maricopa Integrated Health System is using the evaluation results and the major "lessons learned."

Dissemination and Use of Evaluation Findings

Maricopa Integrated Health System shared copies of the final evaluation report with each clinic's medical staff, the Title I grantee (Maricopa County Department of Public Health Services), and the Title II grantee (Office of HIV/AIDS Services, Arizona Department of Health Services). Follow-up discussions with McDowell clinicians identified six critical data elements that were not being systematically recorded. **These data elements included:**

1) Date of earliest HIV-positive diagnosis;

2) Date of entry into clinic;

3) Nadir (lowest) CD4$^+$ lymphocyte count;

4) Diagnostic codes at each patient encounter;

5) Clinical trials start and stop dates; and

6) Causes of treatment failure.

With financial support from a Title III supplemental grant, McDowell now is expanding the electronic clinical database developed during the evaluation to include comprehensive data on all patients seen at the clinic since January 1996. This expanded database will be used to conduct ongoing studies of the therapeutic efficacy and cost effectiveness of treatments and to compare McDowell's therapeutic outcomes with those of other HIV care providers. Patient encounter forms also are being revised to encourage better documentation of primary, secondary, and tertiary diagnoses.

The evaluation revealed a large number of treatment failures among patients on triple therapy. Because medical records often did not indicate the reasons for these failures, the study team was unable to assess the importance of patient non-adherence as a contributing factor. A new study, supported by Title III supplemental funds, is examining how health-related quality of life and the use of alternative and complementary medicines are related to antiretroviral therapy adherence among McDowell patients.

Maricopa Integrated Health System maintains a computerized billing system that tracks all patient encounters. Evaluation data on physician visits and laboratory tests helped validate the utilization data in this billing system. Maricopa representatives now are working with an actuarial firm to examine resource use and cost by disease stage. These cost data will help Maricopa negotiate managed care contracts with eight additional AHCCCS plans. Contracts with all AHCCCS plans will improve continuity of care by enabling uninsured patients who become eligible for AHCCCS during hospitalization to return to McDowell after discharge.

Lessons Learned

This study of HAART utilization and outcomes in two Title III-funded clinics makes an important contribution to clinical knowledge and to our understanding of the "real-world" challenges of outcomes evaluation. When asked what they had learned about the conduct of outcomes evaluations, the principal investigator and the grant administrator offered four observations.

Lesson #1

Clinical outcomes evaluations can be designed and conducted at relatively low cost. By arranging for a graduate student to direct the study, Maricopa Integrated Health System was able to conduct the evaluation for less than $40,000. **The itemized budget was as follows:**

Contract with University of Arizona	
Principal investigator	18,000
Faculty advisor	4,000
Database development/entry	1,500
Communications/travel/supplies	1,104
Indirect costs (7.5%)	1,846
Total	$26,450
Medical Record Abstraction	
Medical records technicians	6,000
Travel	~2,000
Total	$8,000
In-Kind Contributions	~2,000
Total Cost	**$36,450**

The principal investigator pointed out that most graduate students are interested in designing and conducting evaluations that meet dissertation or thesis requirements. The lower fees charged by graduate students may give the impression that they are an inexpensive resource. However, significant staff time must be invested in reviewing their work, providing feedback, and monitoring progress. Organizations should consider the types and amounts of staff support that will be required when budgeting for student-directed evaluations. As an alternative, program staff may wish to conduct the evaluation, with an external evaluator serving in an advisory role.

Lesson #2

The six-month time period allotted for this study was too short. **The estimated times spent on each phase of the study were as follows:**

Phase	Time Spent
Study design and sample selection	1 month
Training and monitoring of medical records technicians	1 week
Medical record abstraction	3 months
Data analysis	1 month
Report preparation	1 month

None of these time frames were regarded as adequate. However, the principal investigator expressed particular concern about the brief time allotted for data analysis. The grant administrator commented on the need to allow adequate time for "administrative preliminaries," such as the issuance of a Request for Proposal, legal reviews, and contract negotiation and signing. If evaluators plan to collect data on human subjects for research purposes, appropriate institutional review boards (IRBs) will need to review and approve the study's objectives, procedures, and method of obtaining informed consent before the evaluation begins. Evaluators should consider IRB requirements and meeting schedules when developing study timetables.

Lesson #3

Varied skills are needed to design and conduct "successful" outcomes evaluations. Evaluators should be familiar with the relevant scientific literature and the ways in which patients at the study clinics may differ from those observed in clinical trials. Evaluation team members should include a committed principal investigator, persons with research design and statistical expertise, and people with HIV/AIDS who can assist with the design and interpretation of the study. Medical record abstracters should be well trained and closely monitored to minimize measurement error. Ideally, medical record abstracters should participate in the design and pilot testing of the medical record abstraction tool.

Lesson #4

Contracts with external evaluators, such as universities and consulting firms, should clearly specify the study's objectives, evaluation questions, timetable, and expected "deliverables." Evaluations should focus on a few key objectives that can be accomplished within the allotted budget and timeframe. Once the contract is executed, study sponsors should be prepared to spend considerable time reviewing the study design, analysis plan, data collection and sampling strategies, evaluation instruments, and draft reports.

Appendix

Table 2. Patient Demographics by Clinic

Demographic Group	El Rio (n=237) No. (%)	McDowell (n=254) No. (%)	χ^2	Degrees of Freedom	p value
Gender					
Females	38 (16)	31 (12)			
Males	199 (84)	223 (88)	1.48	1	0.22
Race/Ethnicity					
White, not Hispanic	143 (60)	167 (66)			
Black, not Hispanic	17 (7)	30 (12)			
Hispanic	76 (32)	51 (20)			
Asian/Pacific Islander	0 (0)	1 (0.4)			
American Indian/ Alaskan Native	1 (0.4)	3 (1)			
Unknown/unreported	0 (0)	2 (1)			
Mode of Exposure[1]					
MSM	145 (61)	140 (55)			
IVDU	55 (23)	28 (11)			
MSM/IVDU	4 (2)	15 (6)			
Heterosexual	17 (7)	44 (17)			
Other/not reported	16 (7)	27 (11)			

[1] Mode of exposure: MSM = men who have sex with men; IVDU = intravenous drug user

Note: Percentages may not add to 100 due to rounding.

Table 3. Patient Characteristics by Clinic

Characteristic Group	El Rio (n=237) No. (%)	McDowell (n=254) No. (%)	χ^2	Degrees of Freedom	p value
Comorbidities					
Intravenous drug use	45 (17)	46 (17)			
Chronic mental illness	22 (8)	13 (5)	2.48	2	0.29
AIDS-defining opportunistic infections at baseline[1]					
None	206 (87)	226 (89)			
Brain lymphoma	0 (0)	0 (0)			
Cerebral toxoplasmosis	1 (0.4)	1 (0.4)			
CMV retinitis/other sites	1 (0.4)	0 (0)			
Cryptococcosis	2 (1)	0 (0)			
Coccidiodomycosis	9 (3)	7 (3)			
Mycobacterium/atypical	5 (2)	3 (1)			
Kaposi's sarcoma	4 (2)	3 (1)			
HIV wasting	1 (0.4)	5 (2)			
Pneumocystis carinii pneumonia	13 (5)	13 (5)			
Progressive multifocal leukoencephalopathy	0 (0)	0 (0)	0.27	1	0.60[3]
Disease severity at baseline[2]					
AIDS-defined	63 (27)	49 (19)	3.70	1	0.05
Asymptomatic/Symptomatic	174 (73)	205 (81)			
Patient status					
Remained in study	182 (77)	162 (64)	9.89	1	0.002
Dropped out of study	55 (23)	92 (36)			
Reason for drop out					
Mortality	19 (35)	10 (11)			
Nursing home admission	2 (4)	0 (0)			
Moved out of area	12 (22)	20 (22)			
Change of insurance status	2 (4)	12 (13)			
Unknown/not reported	20 (36)	50 (54)			

[1] Because some patients had more than one opportunistic infection, the total percentage for each clinic may exceed 100%.

[2] Patients with at least one documented AIDS-defining opportunistic infection and/or $CD4^+$ lymphocyte count less than or equal to 200

[3] Chi-square on total number of AIDS-defining opportunistic infections by treatment site

Note: Percentages may not add to 100 due to rounding.

Table 4. Patient Demographics by Treatment Type

Demographic Group	Triple Therapy[1] (n=268) No. (%)	Non-Triple Therapy (n=223) No. (%)	χ^2	Degrees of Freedom	p value
Gender					
Females	37 (14)	32 (14)	0.03		
Males	231 (86)	191 (86)		1	0.86
Race/Ethnicity					
White, not Hispanic	168 (63)	142 (64)			
Black, not Hispanic	18 (7)	29 (13)			
Hispanic	79 (30)	48 (22)			
Asian/Pacific Islander	0 (0)	1 (1)			
American Indian/ Alaskan Native	2 (1)	2 (1)			
Unknown/unreported	1 (0.4)	1 (1)			
Mode of Exposure[2]					
MSM	167 (62)	118 (53)			
IVDU	40 (15)	43 (19)			
MSM/IVDU	8 (3)	11 (5)			
Heterosexual	31 (12)	30 (13)			
Other/not reported	22 (8)	21 (9)			

[1] The triple therapy group includes patients who received a regimen of at least three antiretroviral drugs, including at least one protease inhibitor, at any time during the study period. The non-triple therapy group includes all patients not meeting the triple therapy group criteria.

[2] Mode of exposure: MSM = men who have sex with men; IVDU = intravenous drug user

Note: Percentages may not add to 100 due to rounding.

Table 5. Patient Characteristics by Treatment Type

Characteristic Group	Triple Therapy[1] (n=268) No. (%)	Non-Triple Therapy (n=223) No. (%)	χ^2	Degrees of Freedom	p value
Comorbidities					
Intravenous drug use	42 (14)	49 (21)			
Chronic mental illness	21 (7)	14 (6)	4.07	2	0.13
AIDS-defining opportunistic infections at baseline[2]					
None	223 (83)	208 (93)			
Brain lymphoma	0 (0)	0 (0)			
Cerebral toxoplasmosis	2 (1)	0 (0)			
CMV retinitis/other sites	1 (0.3)	0 (0)			
Cryptococcosis	1 (0.3)	1 (0.4)			
Coccidiodomycosis	10 (3)	6 (3)			
Mycobacterium/atypical	5 (2)	3 (1)			
Kaposi's sarcoma	4 (1)	3 (1)			
HIV wasting	5 (2)	1 (0.4)			
Pneumocystis carinii pneumonia	17 (6)	9 (4)			
Progressive multifocal leukoencephalopathy	0 (0)	0 (0)	3.52	1	0.06[4]
Disease severity at baseline[3]					
AIDS-defined	79 (29)	33 (15)			
Asymptomatic/Symptomatic	189 (71)	190 (85)	14.90	1	0.001
Patient status					
Dropped out of study	48 (18)	99 (44)			
Remained in study	220 (82)	124 (56)	40.70	1	0.001
Reason for drop out					
Mortality	7 (15)	22 (22)			
Nursing home admission	2 (4)	0 (0)			
Moved out of area	10 (21)	22 (22)			
Change of insurance status	6 (13)	8 (8)			
Unknown/not reported	23 (48)	47 (48)			

[1] The triple therapy group includes patients who received a regimen of at least three antiretroviral drugs, including at least one protease inhibitor, at any time during the study period. The non-triple therapy group includes all patients not meeting the triple therapy group criteria.
[2] Because some patients had more than one opportunistic infection, the total percentage for each treatment type may exceed 100%.
[3] Patients with at least one documented AIDS-defining opportunistic infection and/or $CD4^+$ lymphocyte count less than or equal to 200
[4] Chi-square on total number of AIDS-defining opportunistic infections by treatment type

Table 6. Proportion of Patients Receiving Triple Therapy by Clinic During Total Study Period

	El Rio (n=237)	McDowell (n=254)	χ^2	Degrees of Freedom	p value
Triple Therapy	63% (149)	47% (119)			
Non-Triple Therapy	37% (88)	53% (135)	12.69	1	0.001

Table 7. Proportion of Patients Receiving Triple Therapy by Clinic During Each Qtr.

	El Rio	McDowell
1st Qtr. 1996	11% (26/237)	0.79% (2/254)
2nd Qtr. 1996	20% (47/231)	4% (9/243)
3rd Qtr. 1996	28% (63/227)	9% (21/237)
4th Qtr. 1996	38% (81/216)	13% (29/221)
1st Qtr. 1997	48% (102/212)	24% (51/212)
2nd Qtr. 1997	62% (125/203)	36% (71/196)
3rd Qtr. 1997	71% (132/187)	60% (104/174)

Table 8. Proportion of Patients Within Disease Severity Category at Initiation of Triple Therapy by Clinic

	El Rio (n=149)	McDowell (n=119)	χ^2	Degrees of Freedom	p value
Asymptomatic/ Symptomatic	74 (50%)	44 (37%)			
AIDS-defined	75 (50%)	75 (63%)	4.32	1	0.04

Table 9. Proportion of Asymptomatic/Symptomatic Patients by Clinic and Treatment Type

	El Rio	McDowell	χ^2	Degrees of Freedom	p value
Triple Therapy	74 (56%)	44 (31%)			
Non-Triple Therapy	59 (44%)	99 (69%)	17.44	1	0.001

Table 10. Proportion of AIDS-Defined Patients by Clinic and Treatment Type

	El Rio	McDowell	χ^2	Degrees of Freedom	p value
Triple Therapy	75 (72%)	75 (68%)			
Non-Triple Therapy	29 (28%)	36 (32%)	0.53	1	0.47

Table 11. Mean (SD) Viral Load and Mean (SD) CD4⁺ Lymphocyte Count at Initiation of Triple Therapy by Clinic[1]

	El Rio (n=149)	McDowell (n=119)	χ^2	Degrees of Freedom	p value
Log of viral load	4.03 (0.83)	4.25 (1.0)	1.96	257	0.05
CD4⁺ lymphocyte count	213 (39)	187 (41)	1.15	261	0.25

[1] Normal distributions were achieved by transforming the viral load and CD4⁺ lymphocyte count laboratory data. Analysis of viral load was performed after $\log_{10}$ transformation of the data. Analysis of CD4⁺ lymphocyte count was performed after square root transformation of the data.

Table 12. Mean (SD) of Clinical Variables by Clinic During Total Study Period

	El Rio	McDowell	t statistic	Degrees of Freedom	p value
Log of viral load	(n=216) 3.99 (0.64)	(n=231) 4.09 (0.8)	-1.34	466	0.18
CD4⁺ lymphocyte count	(n=230) 249 (44)	(n=238) 261 (446)	-0.62	397	0.54
AIDS-defining opportunistic infections[1]	(n=237) 0.18 (0.59)	(n=254) 0.11 (0.36)	1.69	381	0.09
AIDS-defining opportunistic infections[2]	(n=237) 0.07 (0.34)	(n=254) 0.02 (0.15)	1.83	323	0.06

[1] Includes all opportunistic infections documented during study period

[2] Excludes all opportunistic infections that preceded the initiation of triple therapy

Table 13. Mortality Rate by Clinic During Total Study Period

	El Rio (n=237)	McDowell (n=254)	χ^2	Degrees of Freedom	p value
Mortality	8% (19)	4% (10)			
No Mortality	92% (218)	96% (244)	3.67	1	0.06

Table 14. Log of Mean (SD) Viral Load Per Patient by Clinic During Each Qtr.

	El Rio	McDowell	t statistic	Degrees of Freedom	p value[1]
1st Qtr. 1996	(n=5) 4.87±0.36 (0.80)	(n=31) 4.74±0.11 (0.91)	0.48	34	0.64
2nd Qtr. 1996	(n=47) 4.39±0.12 (0.85)	(n=50) 4.70±0.08 (0.53)	-2.09	77	0.04
3rd Qtr. 1996	(n=107) 4.25±0.09 (0.95)	(n=75) 4.45±0.07 (0.65)	-1.75	180	0.08
4th Qtr. 1996	(n=104) 4.09±0.10 (0.97)	(n=93) 4.49±0.06 (0.57)	-3.53	169	<0.001
1st Qtr. 1997	(n=137) 3.93±0.08 (0.91)	(n=112) 3.87±0.77 (0.82)	0.57	247	0.57
2nd Qtr. 1997	(n=129) 3.72±0.08 (0.95)	(n=124) 3.72±0.07 (0.75)	-0.06	242	0.95
3rd Qtr. 1997	(n=115) 3.63±0.09 (0.99)	(n=121) 3.68±0.07 (0.75)	-0.40	211	0.69

[1] In order to reduce the risk of a Type I error (rejecting the null hypothesis when it is true), the alpha level was adjusted to 0.007 using the Bonferroni correction. Using this adjusted alpha, El Rio's mean viral load per patient was significantly lower than McDowell's only in the fourth qtr. of 1996.

Table 15. Mean (SD) CD4+ Lymphocyte Count Per Patient by Clinic During Each Qtr.[1]

	El Rio	McDowell	t statistic	Degrees of Freedom	p value[2]
1st Qtr. 1996	(n=78)	(n=74)			
	215	280			
	(39)	(44)	-1.99	148	0.04
2nd Qtr. 1996	(n=99)	(n=68)			
	258	275			
	(48)	(59)	-0.45	165	0.65
3rd Qtr. 1996	(n=98)	(n=83)			
	239	282			
	(45)	(45)	-1.32	179	0.19
4th Qtr. 1996	(n=105)	(n=78)			
	231	222			
	(46)	(43)	0.30	181	0.76
1st Qtr. 1997	(n=142)	(n=99)			
	275	249			
	(46)	(39)	0.97	239	0.34
2nd Qtr. 1997	(n=146)	(n=97)			
	283	280			
	(38)	(46)	-0.09	241	0.93
3rd Qtr. 1997	(n=119)	(n=82)			
	287	304			
	(43)	(32)	-0.56	199	0.58

[1] Square root transformation of data performed for analysis

[2] Bonferroni correction results in adjusted alpha=0.007

Table 16. Mean Number of AIDS-Defining Opportunistic Infections Per Patient by Clinic During Each Qtr.

	El Rio	McDowell	t statistic	Degrees of Freedom	p value[1]
1st Qtr. 1996	0.037 (9/237)	0.024 (6/254)	0.86	425	0.39
2nd Qtr. 1996	0.043 (10/231)	0.025 (6/243)	1.04	407	0.30
3rd Qtr. 1996	0.026 (6/227)	0.004 (1/237)	1.93	295	0.05
4th Qtr. 1996	0.037 (8/216)	0.032 (7/221)	0.22	435	0.82
1st Qtr. 1997	0.018 (4/212)	0.014 (3/212)	0.38	413	0.70
2nd Qtr. 1997	0.024 (5/203)	0.005 (1/196)	1.40	262	0.16
3rd Qtr. 1997	0.005 (1/187)	0.011 (2/174)	-0.63	303	0.53

[1]Bonferroni correction results in adjusted alpha value=0.007

Table 17. Mortality Rates by Clinic During Each Qtr.

	El Rio	McDowell
1st Qtr. 1996	1.7% (4/237)	1.6% (4/254)
2nd Qtr. 1996	1.3% (3/231)	0.0% (0/243)
3rd Qtr. 1996	1.3% (3/227)	0.4% (1/237)
4th Qtr. 1996	1.8% (4/216)	0.0% (0/221)
1st Qtr. 1997	0.9% (2/212)	0.9% (2/212)
2nd Qtr. 1997	0.5% (1/203)	1.5% (3/196)
3rd Qtr. 1997	0.5% (1/187)	0.0% (0/174)

Table 18. Mean (SD) of Clinical Variables by Treatment Type During Total Study Period

	Triple Therapy	Non-Triple Therapy	t statistic	Degrees of Freedom	p value
Log of viral load	(n=259) 4.08 (0.73)	(n=188) 3.98 (0.79)	-1.47	445	0.14
CD4⁺ lymphocyte count[1]	(n=263) 200 (48)	(n=205) 336 (48)	6.87	401	<0.001
AIDS-defining opportunistic infections[2]	(n=268) 0.21 (0.58)	(n=223) 0.07 (0.33)	-3.31	381	0.001
AIDS-defining opportunistic infections[3]	(n=268) 0.03 (0.18)	(n=223) 0.07 (0.33)	1.67	331	0.09

[1] Square root transformation of data performed for analysis

[2] Includes all opportunistic illnesses documented during study period

[3] Excludes opportunistic infections that preceded the initiation of triple therapy

Table 19. Mortality Rates by Treatment Type During Total Study Period

	Triple Therapy (n=268)	Non-Triple Therapy (n=223)	χ^2	Degrees of Freedom	p value
Mortality	3% (7)	10% (22)			
No Mortality	97% (259)	90% (13)	11.52	1	0.001

Table 20. Mean (SD) Number of HIV-Related Health Care Resources Used Per Patient by Clinic

	El Rio (n=237)	McDowell (n=254)	t statistic	Degrees of Freedom	p value
Outpatient physician visits	10.01 (6.81)	7.59 (5.58)	4.30	457	<0.001
CD4⁺ laboratory tests	3.87 (2.26)	2.52 (1.76)	7.34	446	<0.001
Viral load laboratory tests	3.38 (2.30)	2.90 (2.00)	2.45	470	0.015
Hospital admissions	0.56 (1.04)	0.26 (0.67)	3.79	394	<0.001
Emergency room visits	0.25 (0.70)	0.06 (0.30)	3.86	313	<0.001

Table 21. Mean (SD) Number of HIV-Related Health Care Resources Used Per Patient by Treatment Type

	Triple Therapy (n=268)	Non-Triple Therapy (n=223)	t statistic	Degrees of Freedom	p value
Outpatient physician visits	10.65 (6.50)	6.49 (5.26)	-7.83	489	<0.001
CD4⁺ laboratory tests	3.82 (2.17)	2.39 (1.79)	-8.00	489	<0.001
Viral load laboratory tests	3.88 (2.11)	2.23 (1.85)	-9.25	489	<0.001
Hospital admissions	0.41 (0.95)	0.39 (0.78)	-0.15	489	0.877
Emergency room visits	0.13 (0.45)	0.17 (0.63)	0.88	393	0.380

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