

A Public Health Approach to Rapid Scale-Up of Antiretroviral Treatment in Malawi During 2004–2006

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INTRODUCTION

In 2003, Malawi, a resource-limited country in sub-Saharan Africa with a population of 13.6 million, had an adult HIV seroprevalence of 14% with approximately 1 million persons living with HIV/AIDS.¹ In 2004, an estimated 170,000 persons were in need of antiretroviral treatment (ART). National scale-up of free ART, funded primarily by the Global Fund to Fight AIDS, Tuberculosis, and Malaria, began in June 2004.² Influenced by the success of the tuberculosis (TB) directly observed therapy—short-course program, which is based on case finding, standardized treatment regimens, and simplified monitoring and evaluation of patient outcomes, and spurred by a dire shortage of human resources in the health sector, Malawi adopted a public health approach to rapidly scale up HIV treatment services.^{2–7}

This approach, which is characterized by simplified clinical decision making, standardized ART regimens, non-physician care, limited laboratory support, and centralized monitoring and evaluation, resulted in more than 141,000 persons being initiated on ART in the public sector by December 31, 2007.⁸ Those initiated on ART represent about two thirds of patients estimated to be eligible for ART (A. D. Harries, MD, written personal communication 2008). Although a few facilities in Malawi receive external technical and financial support from international organizations, such as Médecins Sans Frontières,⁹ government health care workers are the sole providers in most ART clinics. As of December 31, 2007, 45 private sector sites had initiated ART, based on the national clinical guidelines and monitoring and evaluation tools, for more than 5400 patients.

The World Health Organization (WHO) has recommended a public health approach to scale up ART services in resource-limited countries. However, trends in national ART program outcomes have not been previously reported from sub-Saharan Africa. We examined trends in 4 measures of program quality, including treatment access, key early clinical outcomes, such as mortality, program retention, and 6- and 12-month survival probability during a 27-month period of the ART program in Malawi to determine whether the public health approach to rapid scale-up of ART has been successful.

METHODS

The National ART Guidelines

In Malawi, the first-line ART regimen is a fixed-dose combination tablet of stavudine, lamivudine, and nevirapine that is taken twice daily.¹⁰ Adults and children older than

Background: Approximately 1 million people are infected with HIV in Malawi, where AIDS is the leading cause of death in adults. By December 31, 2007, more than 141,000 patients were initiated on antiretroviral treatment (ART) by use of a public health approach to scale up HIV services.

Methods: We analyzed national quarterly and longitudinal cohort data from October 2004 to December 2006 to examine trends in characteristics of patients initiating ART, end-of-quarter clinical outcomes, and 6- and 12-month survival probability.

Findings: During a 27-month period, 72,666 patients were initiated on ART, of whom about two-thirds were women. The percentage of patients initiated on ART who were children and farmers increased from 5.5% to 9.0% and 23% to 32%, respectively ($P < 0.001$ for trends). Estimated survival probability ranged from 85% to 88% at 6 months and 81% to 84% at 12 months on ART.

Interpretation: In Malawi, a public health approach to ART increased treatment access and maintained high 6- and 12-month survival. Resource-limited countries scaling up ART programs may benefit from this approach of simplified clinical decision making, standardized ART regimens, nonphysician care, limited laboratory support, and centralized monitoring and evaluation.

Key Words: public health approach, antiretroviral treatment, outcomes, national, sub-Saharan Africa, survival

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We declare that we have no conflicts of interest in regard to the findings contained in this article.

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18 months are eligible for ART if they are HIV-positive and are in WHO clinical stage III or IV or stage I or II and have a CD4 T-lymphocyte count <250 cells per cubic millimeter for adults or below the threshold value for children.^{10,11} Children less than 18 months are eligible for ART based on HIV seropositivity, WHO stage, and clinical condition.

The National Monitoring and Evaluation System

In ART clinics, adults and children are followed monthly and vital data are recorded at each visit by use of standardized monitoring tools.^{4,6,7} The principal ART monitoring tools are a patient register and a patient master card. The registers and master cards are kept in the ART clinics, and the patient master cards are maintained in an ordered sequence inside polypropylene sheet protectors in hardcover ring binders. Patient information captured by these tools includes a unique, site-specific ART registration number, age, sex, occupation (a proxy for socioeconomic status), HIV test date and place, reason for starting ART, key opportunistic infections, and the drug regimen. When patients return for follow-up each month, the patient master cards are completed and standardized clinical outcomes, including alive on ART, dead, default (lost to follow-up for more than 90 days), transferred out, and stopped treatment, are recorded. Cumulative and quarterly cohort reports, generated from nonoverlapping intervals, are based on recorded data, which are reviewed for accuracy during quarterly supervision visits to all ART sites. The number of patients in each quarterly cohort includes double-counting of patients who transferred, estimated to be about 10% of all patients registered.⁹ Patients who initiated ART before October 1, 2004, were retrospectively included in the cumulative and initial 12-month longitudinal cohorts.

Patients newly initiated on ART during the quarter are followed over time, and survival outcomes are assessed at 6 and 12 months. For example, the first longitudinal cohort started ART between April 1 and June 30, 2004, and 6- and 12-month outcomes were censored on December 31, 2004, and June 30, 2005, respectively. Six- and 12-month patient outcome data were not censored during the first (October 1 to December 31, 2004) and second (January 1 to March 31, 2005) quarters because the national monitoring and evaluation system was not in place for patients initiating ART before October 1, 2004. Some ART clinics have active patient tracking systems for default patients but most do not because of limited resources. Each patient keeps an ART identity card, which contains his or her unique ART registration number and other related information, including ART drug regimen and initiation date.

In July 2006, the Ministry of Health initiated quarterly assessments of data quality. High performing ART facilities are given certificates of excellence. For the following analyses, patient retention in Malawi was defined as whether a patient remains alive on ART or has been officially transferred out after a specified follow-up interval, consistent with published standards.¹²

Statistical Analysis

Mixed-effects logistic regression models with random effects on the intercept to account for clustering of patients

within facilities were used to analyze both linear trends in aggregate facility-level quarterly cohort data, including baseline patient demographic and clinical characteristics and end-of-quarter outcomes and nonlinear trends in 6- and 12-month longitudinal cohort survival data. The nonlinear trend analysis was selected to estimate survival probability because the median time trend was nonlinear. Data were analyzed by use of PROC GLIMMIX (SAS Institute, Cary, NC).¹³ Aggregate response variables were specified as sample proportions, using events/trials syntax, where events are the number of patients experiencing or reporting an outcome and trials are the total number of patients.¹⁴ In the multivariate analysis, region (north, central, and south), patient enrollment target (low: 25 new patients on ART per month, medium: 50 new patients per month, and high: 150 new patients per month),⁸ facility type (governmental or nongovernmental), and quality of routine data collection (excellent or standard) were controlled for and adjusted odds ratios (AORs) provided.

Survival probabilities were calculated by use of the actuarial method.¹⁴ Patients who defaulted, transferred out, or stopped treatment during a 6- or 12-month period were considered at risk for half of the interval, 3 and 6 months, respectively. To model trends in these survival probabilities by use of the events/trials syntax, each survival probability was converted to an aggregate sample proportion by multiplying the survival probability by the total number assessed at the beginning of the interval minus half of those who defaulted, stopped treatment, or transferred out. This product gave the number of events or rather the number alive at the end of the interval, after adjusting for censoring. Trials were based on the above denominator. Reported *P* values were based on 2-sided tests.

Ethical Review

The evaluation was exempted from ethical review by the National Health Sciences Research Committee in Malawi and the US Centers for Disease Control and Prevention because this study was designed for program monitoring and evaluation.

RESULTS

The total number of HIV-infected patients registered for ART at public clinics in Malawi by December 31, 2006, was 81,821 (Table 1). Of these patients, 57,356 (70%) were known to be on ART and 7364 (9%) had transferred to another site, thus nationally 79% of patients remained on treatment. Eleven percent of patients had died, 9% were lost to follow-up, and 1% stopped treatment.

Standardized, routine, national ART data collection began on October 1, 2004, at 23 public sector ART sites. During the period, October 1, 2004, and December 31, 2006, a total of 72,666 patients were registered at 104 ART sites and were included in the following analysis.

Access to Treatment

From quarter 1 (October 1 to December 31, 2004) through quarter 9 (October 1 to December 31, 2006), percentages of patients initiating ART who were women were 60%–63%,

TABLE 1. Baseline Characteristics and Outcomes of the Cumulative Cohort of HIV-Infected Patients Initiated on ART in Malawi Through December 31, 2006 (N = 81,821)*

Characteristic	n (%)
Sex	
Female	50,162 (61)
Age	
Adults aged ≥15 yrs	76,058 (93)
Occupation (n = 78,950)†	
Housewife	15,745 (20)
Farmer	19,415 (25)
Military	1134 (1)
Health care worker	1289 (2)
Other	41,367 (52)
Reasons for starting ART	
Stage III	53,030 (65)
Stage IV	18,958 (23)
Stage I and II with CD4 count <250 cells/μL	9833 (12)
TB status at ART initiation	
Active or prior TB disease	13,308 (16)
Outcomes	
Alive and on ART	57,356 (70)
Dead	9327 (11)
Lost to follow-up	7753 (9)
Stopped treatment	365 (<1)
Transferred out	7364 (9)
Current ART regimen of patients alive and on ART (n = 57,356)	
First-line regimen	55,518 (97)
Alternative first-line regimen	1690 (3)
Second-line regimen	148 (0)
Ambulatory status (n = 51,440)†	
Ambulatory	50,551 (98)
Work status (n = 51,440)†	
Working	49,490 (96)
Side effects (n = 46,969)†	
Significant side effects	2132 (5)
Adherence (n = 38,426)†	
Pill count showing ≥95% adherence	35,736 (93)
Time of death (n = 9327)	
First month	3207 (34)
Second month	2069 (22)
Third month	1100 (12)
After the third month	2951 (32)

*This number includes 9155 patients initiated on ART before October 1, 2004, and an estimated 10% double-counting of patients who transferred out.

†Smaller denominator due to missing data.

whereas percentages of children and subsistence farmers increased from 5.5% to 9.0% ($P < 0.0001$ for trend), and from 23% to 32% ($P < 0.0001$ for trend), respectively (Table 2). The percentage of patients who were started on ART because they were in WHO clinical stage IV decreased from 26% to 21% during this period ($P < 0.001$ for trends), whereas the trend in the percentage of patients who initiated ART who were in stage I or II with CD4 cell count <250 cells per microliter increased from quarter 1 to quarter 9 ($P < 0.001$ for trends). The estimated percentage of patients starting ART who had active TB disease or a prior history of TB within 2 years varied between 10% and 18%.

Early Clinical Outcomes

During October 2004 to December 2006, by the end of the quarter of treatment initiation (average duration of treatment = 6 weeks), the percentage of those known to have died was between 3% and 5% and the percentage of patients known to be alive and on ART was between 93% and 96%, whereas the percentage of patients transferred out increased from <1% to 2% ($P < 0.0001$ for trend) (Table 3). Of those patients alive at the end of the quarter, the percentage of patients who remained on the first-line regimen was about 99% and the percentage of patients whose end-of-quarter functional status was reported as ambulatory was from 96% to 99%, with 89%–94% of patients reportedly working. Patient adherence ≥95% was between 93% and 97% for the 47,405 (65%) who had their pill counts assessed.

Survival Probability

Longitudinal cohort data at 6 and 12 months were available for 7 of 9 quarterly cohorts (Table 4). The trend in 6- and 12-month survival probability estimates followed U-shaped patterns. Six-month survival probability decreased from 87% in quarter 1 to 85% in quarter 4 and then increased to 88% in quarter 7 ($P < 0.05$ linear; $P < 0.01$ quadratic) (Fig. 1). Twelve-month survival probability decreased from 84% in quarter 1 to a nadir of 81% in quarter 5 and increased to 82% in quarter 7 ($P < 0.01$ linear; $P < 0.01$ quadratic).

Analysis of Facility Characteristics

In multivariate analysis, location in the southern region [AOR 0.74; confidence interval (CI): 0.60 to 0.91], low patient enrollment (AOR 0.72; CI: 0.54 to 0.94), and being a government site (AOR 0.65; CI: 0.52 to 0.82) were facility-level characteristics associated with lower 6-month survival probability, although not having received a certificate of excellence for routine data collection was of borderline significance (AOR 0.83; CI: 0.69 to 1.01), with central region, high patient enrollment, nongovernmental site, and receipt of a certificate of excellence for routine data collection as referent groups, respectively. Low ART patient enrollment and governmental status remained statistically significantly associated with lower 12-month survival probabilities, although not having received a certificate of excellence for routine data collection became significant (AOR 0.75; CI: 0.60 to 0.93), and region was no longer statistically significant.

DISCUSSION

ART is being rapidly scaled up in sub-Saharan Africa. Although the expansion of treatment services has been substantial, many millions of eligible patients remain untreated.¹⁵ To achieve universal ART coverage in Africa, new service delivery models are needed, especially those that facilitate increased access to treatment while ensuring quality. The public health approach to ART, promoted by the WHO and based on the principles of simplified clinical decision making, standardized ART regimens, nonphysician care, limited laboratory support, and centralized monitoring and evaluation, is regarded as a potentially important model;

TABLE 2. Demographic and Clinical Characteristics of Patients Initiating ART by Quarter,* October 1, 2004, to December 31, 2006 (N = 72,666)

Characteristic	1	2	3	4	5	6	7	8	9	Trend	P	Total †
Patients initiated in quarter, n	3261	4530	5696	7784	7775	8880	10,465	12,022	12,253	—	—	72,666
ART sites, n	23	34	53	60	60	67	94	104	104	—	—	104
Sex, n (%)												
Women	1995 (61)	2789 (62)	3391 (60)	4753 (61)	4759 (61)	5414 (61)	6447 (62)	7563 (63)	7623 (62)	+	<0.01	44,734 (62)
Age, n (%)												
Adults	3080 (95)	4327 (96)	5346 (94)	7358 (95)	7341 (94)	8323 (94)	9753 (93)	10,939 (91)	11,144 (91)	—	<0.001	67,611 (93)
Children <15 yrs	181 (5)	203 (4)	350 (6)	426 (5)	434 (6)	557 (6)	712 (7)	1083 (9)	1109 (9)	+	<0.001	5055 (7)
Occupation, n (%)												
Housewife	NA	NA	1010 (23)	1996 (27)	1833 (24)	1985 (23)	2208 (22)	2542 (22)	2638 (22)	—	<0.001	14,904 (23)
Subsistence farmer	NA	NA	1037 (23)	1754 (24)	1985 (26)	2438 (28)	3042 (31)	3685 (32)	3852 (32)	+	<0.001	18,435 (28)
Military/police	NA	NA	124 (3)	144 (2)	93 (1)	125 (1)	156 (2)	152 (1)	147 (1)	—	<0.001	1009 (2)
Teacher	NA	NA	225 (5)	304 (4)	314 (4)	313 (4)	328 (3)	321 (3)	305 (3)	—	<0.001	2261 (4)
Business person	NA	NA	681 (15)	1164 (16)	1233 (16)	1240 (14)	1379 (14)	1674 (15)	1554 (13)	—	<0.001	9369 (14)
Health care worker	NA	NA	98 (2)	160 (2)	147 (2)	131 (2)	151 (2)	155 (1)	134 (1)	—	<0.001	1084 (2)
Student	NA	NA	293 (5)	343 (5)	345 (5)	390 (4)	443 (5)	573 (5)	641 (5)	+	<0.001	3182 (5)
Other	NA	NA	988 (22)	1604 (22)	1774 (23)	2193 (25)	2178 (22)	2429 (21)	2681 (22)	+	0.15	14,440 (22)
ART indication, n (%)												
WHO Stage III	1640 (57)	3007 (63)	3738 (66)	5248 (67)	5247 (67)	6099 (69)	6992 (67)	8101 (67)	7874 (64)	+	<0.001	47,946 (66)
WHO Stage IV	750 (26)	1072 (22)	1461 (25)	1850 (24)	1844 (24)	2007 (22)	2268 (22)	2394 (20)	2600 (21)	—	<0.001	16,246 (22)
CD4 ⁺ cell count <250 cells/ μ L	507 (17)	702 (15)	496 (9)	686 (9)	684 (9)	774 (9)	1205 (11)	1527 (13)	1779 (15)	+	<0.001	8360 (12)
TB status at ART initiation												
Active or prior TB, n (%)	351 (11)	451 (10)	908 (16)	1363 (18)	1186 (15)	1333 (15)	1613 (15)	1748 (15)	1686 (14)	—	0.13	10,639 (15)

NA, not available.

*Quarter 1: October 1 to December 31, 2004; quarter 2: January 1 to March 31, 2005; quarter 3: April 1 to June 30, 2005; quarter 4: July 1 to September 30, 2005; quarter 5: October 1 to December 31, 2005; quarter 6: January 1 to March 31, 2006; quarter 7: April 1 to June 30, 2006; quarter 8: July 1 to September 30, 2006; and quarter 9: October 1 to December 31, 2006.

†Percentages reflect total number initiating ART minus 3043 (4.2%) cumulative patients with missing data.

however, patient outcome data from national ART programs that use this approach are limited.³

Although ART patient outcomes from centers of excellence with private technical support, for example, from international organizations, have been highly encouraging, these sites are usually not nationally representative.^{9,16–23} Malawi, an impoverished country fighting a generalized HIV epidemic with limited health infrastructure and human resources, has used a public health approach to scale up ART.² This approach, which is the result of difficult decisions requiring national consensus, is designed to balance goals of achieving maximal and equitable access to ART and ensuring high-quality care.^{2,3} For example, patients on ART do not receive laboratory monitoring, such as hemoglobin and hematocrit, electrolytes, renal and liver function, and CD4⁺ cell count testing. And clinical officers, not physicians, provide the majority of HIV care and treatment services in Malawi, a task-shifting strategy viewed as critical to ART scale-up.

This report describes 4 measures of success of national rapid scale-up of ART in Malawi: treatment access, key early clinical outcomes, such as mortality, program retention, and 6- and 12-month survival probability. Our findings demonstrate that, during the first 27 months of scale-up, Malawi maintained or improved the quality of national ART services, according to these parameters. Specifically, Malawi increased

the proportion of those starting ART who were children and subsistence farmers, who represent the rural poor, from 5% to 9% and from 23% to 32%, respectively. Additionally, the proportion of patients starting ART without advanced disease progression by WHO clinical staging almost doubled, and the percentage of patients starting ART who had active TB disease or a prior history of TB within 2 years was between 10% and 18%.

Overall, 11% of patients were known to have died, whereas between 3% and 5% of patients died during the quarter of ART initiation. Retention on ART at 6 and 12 months was 80% and 75%, respectively, comparable to mean patient retention from select, subnational ART cohorts in sub-Saharan Africa reported in a recent systematic review.¹³ Documented mortality at 6 and 12 months was 11% and 13%, respectively, whereas the proportion lost to follow-up was 8% at 6 months and 11% at 12 months. Some patients who are lost to follow-up presumably represent undocumented deaths. A study of patients who were lost to follow-up in northern Malawi found that 50% were actually undocumented deaths.²⁴ If this finding is generalizable to the national ART program, true mortality at 6 months would be about 15% at 6 months and 18.5% at 12 months.

Estimated ART patient survival probability was 85%–88% at 6 months and 81%–84% at 12 months. Because 88% of

TABLE 3. End of First Quarter Clinical Outcomes of Patients Initiating ART by Quarter,* October 1, 2004, to December 31, 2006 (N = 72,666)

Characteristic	1	2	3	4	5	6	7	8	9	Trend	P	Total
ART patients initiated in quarter, n	3261	4530	5696	7784	7775	8880	10,465	12,022	12,253	NA	NA	72,666
ART sites, n	23	34	53	60	60	67	94	104	104	NA	NA	104
Clinical status at end of quarter, n (%)†												
Alive on ART	3119 (96)	4294 (95)	5347 (94)	7236 (93)	7279 (94)	8347 (94)	9823 (94)	11,254 (94)	11,542 (94)	+	0.43	68,239 (94)
Dead	117 (4)	151 (3)	237 (4)	395 (5)	350 (5)	399 (5)	415 (4)	507 (4)	449 (4)	-	0.37	3020 (4)
Default‡	NA	NA	NA	NA	NA							
Stopped treatment	14 (<1)	25 (1)	13 (<1)	21 (<1)	30 (<1)	16 (<1)	17 (<1)	21 (<1)	29 (<1)	-	<0.001	186 (<1)
Transferred out	11 (<1)	44 (1)	99 (2)	132 (2)	116 (1)	118 (1)	210 (2)	240 (2)	233 (2)	+	<0.001	1203 (2)
Of patients alive on ART												
ART regimen, n (%)												
First-line regimen	NA	NA	5308 (99)	7198 (99)	7239 (99)	8282 (99)	9718 (99)	11,135 (99)	11,387 (99)	-	<0.001	60,267 (99)
First-line substitution	NA	NA	39 (1)	38 (1)	39 (1)	64 (1)	103 (1)	111 (1)	148 (1)	+	<0.001	542 (1)
Second-line regimen	NA	NA	0	0	1 (<1)	2 (<1)	2 (<1)	7 (<1)	7 (<1)	+	<0.001	19 (<1)
Functional status, n (%)												
Patients assessed	NA	NA	4300 (76)	6654 (86)	7188 (93)	8229 (93)	9487 (97)	10,925 (91)	10,713 (87)	NA	NA	57,496 (91)
Patients reported ambulatory			3552	4239 (99)	6471 (97)	6884 (96)	7978 (97)	9121 (96)	10,657 (99)	+	<0.001	61,794 (85)
Patients reported working	2384	3316	4011 (93)	6094 (92)	6484 (90)	7472 (91)	8448 (89)	10,092 (92)	10,103 (94)	+	0.06	58,044 (80)
Side effects, n (%)												
Patients assessed	NA	NA	3776 (66)	7110 (91)	6656 (86)	7764 (87)	9025 (92)	10,394 (87)	10,347 (85)	NA	NA	55,072 (85)
Patients reporting side effects	83	158	182 (5)	267 (4)	211 (3)	252 (3)	305 (3)	332 (3)	315 (3)	-	0.1936	2105 (3)
Adherence (pill counts), n (%)												
Patients assessed	1755 (54)	3443 (76)	2594 (46)	5440 (70)	5579 (72)	5787 (65)	6957 (67)	7873 (66)	7977 (65)	NA	NA	47,405 (65)
Patients with >95% adherence	1674 (95)	3207 (93)	2496 (96)	5164 (95)	5314 (95)	5602 (97)	6667 (96)	7294 (93)	7598 (95)	-	<0.01	45,016 (95)

*Quarter 1: October 1 to December 31, 2004; quarter 2: January 1 to March 31, 2005; quarter 3: April 1 to June 30, 2005; quarter 4: July 1 to September 30, 2005; quarter 5: October 1 to December 31, 2005; quarter 6: January 1 to March 31, 2006; quarter 7: April 1 to June 30, 2006; quarter 8: July 1 to September 30, 2006; and quarter 9: October 1 to December 31, 2006.

†Average duration of follow-up was 6 weeks (range: 1 day to 3 months).

‡Default defined as lost to follow-up for >90 days; unable to assess by end of quarter.

patients initiated on ART were in WHO clinical stage III or IV, and data from Malawi indicate that an estimated 75% of untreated patients in these advanced stages will die within 12 months, many thousands of lives are being saved by use of ART each year.²⁵ Recent data from Malawi suggest that the introduction of ART reduced overall population-level mortality by 10% in 15- to 59-year-olds in this period.²⁶

Although there seems to have been an initial decline in estimated 6- and 12-month survival during the first few quarters of national scale-up, likely coinciding with the early extension of ART services beyond established centers of excellence, recent trends in estimated survival have increased, suggesting that national stakeholders have managed to keep pace with this expansion and improve quality. Features of the public health approach that have facilitated rapid scale-up of ART services in Malawi include the following: (1) simplified national ART patient monitoring guidelines; (2) standardized ART regimens; (3) a standardized intensive clinical training program, based on the national ART guidelines, and preservice clinical mentoring at experienced ART sites; (4) a structured system of ART site accreditation, before

initiating treatment at a facility; (5) supervision and data quality assurance during quarterly site visits to all ART sites by the HIV Unit of the Ministry of Health and its partners; and (6) a system of supplying drugs to facilities based on Ministry assessments of patient enrollment; and (7) no ART drug stockouts.²⁷

This report profiles the first 27 months of ART scale-up in Malawi, within the “honeymoon” period for first-line antiretroviral drugs. Acquired and transmitted drug resistance remain important concerns, although a recent survey showed low or no prevalence of transmitted drug-resistant mutations.²⁸ Medication adherence, initially presumed to be suboptimal in resource-limited settings, has been considerably better than expected.^{19,29} The national ART patient survival estimates and retention compare favorably with data from centers of excellence in resource-limited settings.^{9,12,21-23,30} Importantly, patients are progressively being initiated on ART with lower clinical staging, which is likely to further increase survival.¹⁸ However, selected groups of sites with lower patient survival probabilities, such as those identified in this study that have fewer ART patients or are located in the southern region, may

TABLE 4. Six- and 12-Month Clinical Outcomes for Patients Initiating ART by Quarter, from April 1, 2004, to June 30, 2006 (n = 48,148 and 32,710, respectively)*

Quarter Censored†	Patients Starting ART, n	Alive and on ART, n (%)	Dead, n (%)	Lost to Follow-Up, n (%)	Transferred, n (%)	Stopped Treatment, n (%)
6-month clinical outcomes‡						
3	3050	2340 (76.7)	271 (8.9)	206 (6.8)	208 (6.8)	25 (0.8)
4	4450	3414 (76.8)	386 (8.7)	284 (6.4)	332 (7.5)	34 (0.8)
5	5527	3939 (71.3)	596 (10.8)	496 (9.0)	472 (8.5)	24 (0.4)
6	7905	5703 (72.1)	972 (12.3)	654 (8.3)	517 (6.5)	59 (0.8)
7	7647	5366 (70.2)	904 (11.8)	809 (10.6)	515 (6.7)	53 (0.7)
8	8961	6411 (71.5)	1092 (12.2)	755 (8.4)	674 (7.5)	29 (0.3)
9	10,608	7861 (74.1)	1130 (10.7)	807 (7.6)	786 (7.4)	24 (0.2)
Total	48,148	35,039 (72.8)	5352 (11.1)	4012 (8.3)	3504 (7.3)	248 (0.5)
12-month clinical outcomes‡						
3§	921	715 (77.6)	98 (10.6)	70 (7.6)	21 (2.3)	17 (1.9)
4	3096	2233 (72.1)	241 (7.8)	237 (7.7)	361 (11.7)	24 (0.7)
5	3081	1916 (62.2)	390 (12.7)	370 (12.0)	376 (12.2)	29 (0.9)
6	4580	2973 (64.9)	580 (12.7)	510 (11.1)	465 (10.2)	52 (1.1)
7	5315	3323 (62.5)	753 (14.2)	474 (8.9)	737 (13.9)	29 (0.5)
8	7846	5014 (64.0)	1213 (15.5)	788 (10.0)	781 (9.9)	50 (0.6)
9	7871	4832 (61.4)	1116 (14.2)	1097 (14.0)	772 (9.8)	54 (0.6)
Total	32,710	21,006 (64.2)	4391 (13.4)	3546 (10.9)	3513 (10.7)	255 (0.8)

*“Six-month” outcomes were for ART patients followed for between 6 and 9 months, and “12-month” outcomes were for ART patients followed for between 12 and 15 months.
 †Censoring dates for: quarter 3—June 30, 2005; quarter 4—September 30, 2005; quarter 5—December 31, 2005; quarter 6—March 31, 2006; quarter 7—June 30, 2006; quarter 8—September 30, 2006; and quarter 9—December 31, 2006.
 ‡Six-month outcomes were reported by 18, 32, 51, and 60 of 60 sites providing ART during quarters 3, 4, 5, and 6, respectively, and by 60, 60, and 96 of 104 sites providing ART during quarters 7, 8, and 9, respectively. Twelve-month outcomes were reported by 6, 14, 21, and 35 of 60 sites providing ART during quarters 3, 4, 5, and 6, respectively, and by 53, 60, and 61 of 104 sites providing ART during quarters 7, 8, and 9, respectively.
 §Twelve-month longitudinal cohorts censored during quarters 3 and 4 included patients initiated on ART before October 1, 2004.

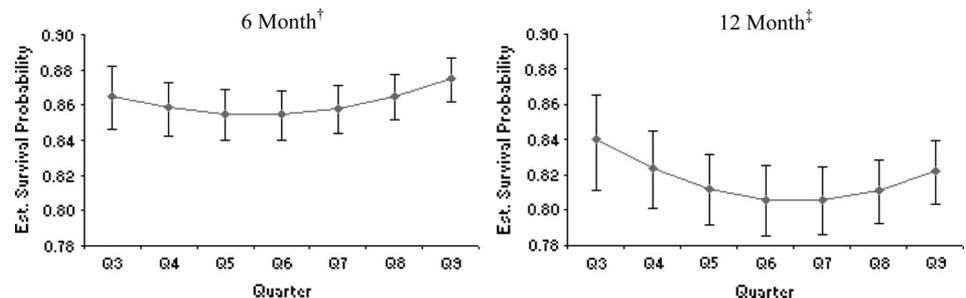
need additional support, ideally provided on a regional basis by established centers of excellence.

Ongoing scale-up toward the goal of universal access to ART will be difficult. Many medium- and large-burden ART sites are currently at or near peak patient carrying capacity. Reliable monitoring and evaluation, essential to rapid scale-up, will become increasingly challenging and will require innovative approaches to ensure data quality.^{29,31–33} Further expansion of ART coverage will require diligence and innovation, including decentralization of services to primary health centers, further task shifting of responsibilities to lower cadres of care providers, and development of novel data collection tools.

Nevertheless, important non-ART interventions, such as co-trimoxazole prophylaxis and insecticide-treated bed nets,

are being scaled up, which should have further beneficial effects on patient survival.^{34–37} Additionally, although 10,639 (23%) of the estimated 47,094 new TB patients who were HIV infected were initiated on ART during the evaluation period, improved linkage between TB and ART programs is essential.⁸ Importantly, substantial numbers of health care workers, critical to the national ART scale-up effort, are accessing ART, with good outcomes.³⁸ Finally, although recent data suggest that national HIV prevalence may be declining, prevalence in rural areas, where the vast majority of Malawians live, seems to be increasing.³⁹ It is important that access to HIV care and treatment services continues to expand and be maximally utilized to enhance national HIV prevention efforts, such as with “prevention for positives” interventions.⁴⁰

FIGURE 1. Six- and 12-month survival probability, based on quarterly* estimates for patients initiating ART in Malawi, October 1, 2004, to March 31, 2006. *For quarterly censoring: quarter 3: April 1 to June 30, 2005; quarter 4: July 1 to September 30, 2005; quarter 5: October 1 to December 31, 2005; quarter 6: January 1 to March 31, 2006; quarter 7: April 1 to June 30, 2006; quarter 8: July 1 to September 30, 2006; and quarter 9: October 1 to December 31, 2006. †P < 0.05 linear; P < 0.01 quadratic; bars represent 95% CIs. ‡P < 0.01 linear; P < 0.01 quadratic; bars represent 95% CIs.



Limitations of these analyses were that data were quarterly, aggregate, and facility level, not patient level, thus restricting the type of analysis. Also, some ART facilities had missing data, particularly early on in the scale-up, which may have biased the results. Additionally, the numbers of patients in quarterly cohorts included double-counting of transfers, estimated at 10% of total registered, which may have led to erroneous estimation of survival probability.

In summary, Malawi has vigorously responded to a nationwide HIV/AIDS epidemic by use of a public health approach to ART scale-up. By ensuring treatment access for vulnerable populations, maintaining low early mortality, and increasing survival, Malawi's national ART program has performed well and had substantial societal impact. This approach represents a relevant paradigm for scale-up of ART in other resource-limited settings which continue to face stark choices between slow scale-up of more robust, resource-intensive service delivery models, as global resources are mobilized, and rapid scale-up with minimal supporting services.

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