



# Distance to care, enrollment and loss to follow-up of HIV patients during decentralization of antiretroviral therapy in Neno District, Malawi: A retrospective cohort study

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1 **Full title: Distance to care, enrollment and loss to follow-up of HIV patients during decentralization of**  
2 **antiretroviral therapy in Neno District, Malawi: A retrospective cohort study**

3 **Short title: Decentralization of ART in Neno, Malawi**

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## Abstract

HIV/AIDS remains the 2nd most common cause of death in low and middle-income countries (LMICs), and only 34% of eligible patients in LMICs received antiretroviral therapy (ART) in 2013. This study investigated the impact of ART decentralization on patient enrollment and retention in rural Malawi. We reviewed electronic medical records of patients registered in the Neno District ART program from August 1, 2006, when ART first became available, through December 31, 2013. We used GPS data to calculate patient-level distance to care, and examined number of annual ART visits and one-year lost to follow-up (LTFU) in HIV care. The number of ART patients in Neno increased from 48 to 4,194 over the decentralization period. Mean travel distance decreased from 7.3 km when ART was only available at the district hospital to 4.7 km when ART was decentralized to 12 primary health facilities. For patients who transferred from centralized care to nearer health facilities, mean travel distance decreased from 9.5 km to 4.7 km. Following a transfer, the proportion of patients achieving the clinic’s recommended  $\geq 4$  annual visits increased from 89% to 99%. In Cox proportional hazards regression, patients living  $\geq 8$  km from a health facility had a greater hazard of being LTFU compared to patients  $< 8$  km from a facility (adjusted HR: 2.0; 95% CI: 1.8—2.3). ART decentralization in Neno District was associated with increased ART enrollment, decreased travel distance, and increased retention in care. Increasing access to ART by reducing travel distance is one strategy to achieve the ART coverage and viral suppression objectives of the 90-90-90 UNAIDS targets in rural impoverished areas.

**Key words:** HIV, ART, decentralization, Malawi, Sub-Saharan Africa, SSA, GIS

48 **Introduction**

49 HIV/AIDS remains a leading cause of death and disability, with over 35 million people infected  
50 worldwide, resulting in 1.5 million deaths annually [1]. Although the Millennium Development Goals  
51 aimed for universal access to antiretroviral therapy (ART) by 2010 [2], in 2013, only a third of those  
52 eligible for ART living in low- and middle-income countries (LMICs) received it [3,4]. In sub-Saharan  
53 Africa (SSA), an estimated 80% of eligible people living with HIV were not receiving ART in 2013 [5].

54 In order to increase access to HIV treatment, many SSA countries have decentralized HIV care  
55 from hospitals to health centers and other primary health facilities closer to the community [6].  
56 Decentralization seeks to reduce distance traveled by patients, task shift ART initiation and HIV  
57 management from physicians to lower-cadre health workers, and integrate delivery of ART within  
58 existing primary health care systems.

59 Malawi, a country of over 16 million people with an adult HIV prevalence of 10.3% and 84% of  
60 its population living in rural areas [7],[8] has prioritized ART decentralization, achieving ART coverage  
61 levels of 80% in 2013 [9]. Neno District is one of the most impoverished and geographically isolated  
62 regions of Malawi. In Neno District, universal HIV testing became available in 2007, and ART care was  
63 decentralized from one district hospital to 12 health facilities between 2006 and 2012, with nurses and  
64 non-physician clinicians assuming primary responsibility for ART service delivery.

65 In Malawi and elsewhere in SSA, ART decentralization has generally improved outcomes [6,10].  
66 Implementation studies from Malawi, South Africa, and Ethiopia have demonstrated that  
67 decentralization leads to improved patient retention and enrollment [10],[11], particularly for stable  
68 adult patients on ART [12]. Decentralization has also been shown to reduce costs by shifting care to  
69 lower-level professionals [13], and to improve access to care for populations from lower socioeconomic  
70 strata [14].

71           Despite the available evidence, gaps remain in our understanding of the effects of initiating and  
72 ART at decentralized facilities [6,10,15] and the associations between this kind of full decentralization  
73 and longitudinal changes in patient behavior and health outcomes [10]. To address these evidence gaps,  
74 we used a geographic information system (GIS) and an electronic medical record (EMR) to track changes  
75 in patients' travel distance, treatment-seeking behavior, and care retention over a five-year period of  
76 ART decentralization in rural Neno District, Malawi. To understand the impact of ART decentralization in  
77 Neno District, we studied its effect on distance-to-care, appointment adherence and loss to follow up  
78 for ART patients between 2006 and 2013.

## 79 **Materials and Methods**

### 80 *ART decentralization and service delivery in Neno*

81           We conducted our study in Neno District, Malawi, a mountainous rural region of 1469 km<sup>2</sup> in the  
82 south of the country with a 2013 population of approximately 137,000 people [16]. In 2007, Partners In  
83 Health/Abwenzi Pa Za Umoyo (PIH/APZU) began a partnership with the Ministry of Health (MOH) to  
84 provide comprehensive, community-based health care in Neno District. PIH/APZU utilizes an  
85 accompaniment model to pair community health workers with persons living with HIV (PLWH), which  
86 has successfully promoted patient retention and favorable clinical outcomes in several resource-  
87 constrained settings, including Neno [17,18]. Between 2006 and the end of 2012, the MOH opened 10  
88 static ART clinics supported by PIH/APZU at primary health facilities throughout the district to  
89 decentralize front-line HIV care (Figure 1). When new ART clinics opened, all patients were invited to  
90 transfer to an ART clinic closer to their home.

91           HIV treatment at Neno District facilities followed national guidelines [19,20]. From 2006 to  
92 2010, HIV-infected patients were ART eligible if they met one of the following criteria: CD4 count <250  
93 cells/mm<sup>3</sup>, WHO Stage 3 or 4 disease, or Stage 2 disease with a total lymphocyte count <1,200 cells/

94 mm<sup>3</sup>. In 2011, Malawi introduced the following new guidelines: an increased CD4 count threshold for  
95 ART initiation (350 cells/mm<sup>3</sup>); initiation of universal lifelong ART for all HIV-infected children under 2  
96 years; and Option B+, which included lifelong ART for all HIV-infected pregnant and breastfeeding  
97 women. Patients who initiated ART visited a health facility every 1-3 months for medical review and to  
98 refill their supply of cotrimoxazole preventative therapy and ART.

### 99 *Study design and population*

100 We performed a retrospective cohort study of all adult and pediatric patients living in Neno  
101 District who initiated ART between August 1, 2006 and December 31, 2013 at any clinic in the district  
102 and had at least two ART visits in this time period.

### 103 *Data source*

104 Malawi's national HIV program uses a paper-based reporting system to collect data on patient  
105 demographics and service provision. In Neno, PIH/APZU augments the MOH system by transcribing the  
106 paper patient data into equivalent electronic forms in an EMR using the OpenMRS platform [21]. We  
107 exported individual-level data, including health facility visit records, and ascertained patient transfers  
108 between health facilities using a unique EMR identifier.

### 109 *Geospatial data collection and analysis*

110 We collected GPS coordinates with a GPSMAP 60CSx device (Garmin, Olathe, Kansas, USA) for  
111 each Neno health facility and each village recognized by the MOH. To ensure patient privacy and  
112 simplify the data collection process, we collected coordinates at the commercial center of each village,  
113 or if no commercial center existed, at the home of the village chief. GPS coordinates were converted to  
114 a shapefile using DNR Garmin version 6. For each patient, we linked their home village reported at ART

115 registration to corresponding GPS coordinates. In our analyses, we excluded patients with missing village  
116 information.

117 For distance analyses, we used both Euclidean distance and cost distance. Euclidean  
118 measurements calculate distance “as the crow flies”, without regard to topography. Cost distance  
119 considers topographical features when calculating distance between two points. Distance analyses were  
120 performed in ArcMap 10.2 and Python 2.7.

### 121 *Statistical analysis*

122 To analyze the impact of full ART decentralization, we divided Neno district’s decentralization  
123 process into five phases based on the following rationale: during phase 1 ART was available only at the  
124 Neno District Hospital; in phase 2 the Lisungwi Community Hospital began to provide ART. During  
125 phases 3 and 4, ART became available at primary health facilities, with 4 facilities providing ART during  
126 phase 3 and an additional 6 during phase 4. Phase 5 captured the six-month period immediately  
127 following full ART decentralization (Figure 1). The ends of the first three phases (31 May 2008, 31  
128 January 2009, and 31 July 2010) correspond to the day prior to the opening of a hospital or clinic in the  
129 next wave of service decentralization. The fourth phase ended on 1 May 2012, six months after the final  
130 health facility began providing HIV treatment, and the final phase ended on 1 November 2012, 6 months  
131 thereafter. The fourth phase also captured the 2011 introduction of Option B+ and guideline shift.

### 132 **Fig 1. ART decentralization timeline.**

133 The timeline displays HIV care in Neno District from August 1, 2006, when public care first became  
134 available, through December 31, 2012. (DH = district hospital, CH = community hospital, HC = health  
135 center, RHC = rural health center)

136  
137 Our primary outcome measures were appointment adherence and loss to follow up.  
138 Appointment adherence is thought to provide a measure of patient engagement in HIV care, and may  
139 predict viral suppression.[22,23] To estimate appointment adherence, we considered that all patients  
140 were recommended to have at least 4 visits per year, and that patients received a 1-3 month supply of

141 ART at each visit, indicating that those with fewer visits may have experienced ART interruption.  
142 Therefore, we conservatively calculated the median number of visits per year for each patient, and  
143 defined patients with fewer than 4 visits per year to be “non-adherent” to appointments.

144 We defined a patient as “lost to follow up (LTFU)” if his or her EMR status was not “alive and on  
145 ART.” This included patients whose vital status was recorded as dead, defaulted, stopped or transferred  
146 out (without a corresponding “transfer in” to a different facility) or if the patient did not have  $\geq 1$   
147 recorded ART visit with 180 days of the relevant time point. We included death and default within our  
148 definition of LTFU to account for previously described high mortality among patients who leave care in  
149 SSA [24]. However, due to our inability to track people who transferred outside of the district who may  
150 have received care, this approach likely resulted in a conservative estimate of patient retention. Non-  
151 LTFU patients were considered “active.”

152 We report descriptive statistics for patients organized by decentralization phase, including the  
153 number of patients enrolled in care at any point during each phase, as well as the number of patients  
154 newly enrolled during each phase. We describe the sub-cohorts of patients that newly initiated ART for  
155 each phase and present their demographic, clinical, and distance information. We defined a patient as  
156 “in care” at the end of a phase if his/her most recent documented status prior to the end of the phase  
157 was “alive and on ART” and if he/she had  $\geq 1$  ART visit within 180 days of the phase date [25].

158 We examined changes in appointment adherence and LTFU one year after enrollment before  
159 and after transfer in the subgroup of patients who transferred at least once during the study period,  
160 matched by patient (before/after transfer), with repeated measures analysis of variance (ANOVA). We  
161 also used t-tests to compare demographic characteristics, annual visits and LTFU between patients who  
162 transferred and those who never transferred.



163 Finally, to assess the association between travel distance and LTFU, we used Cox proportional  
164 hazards regression to estimate the hazard ratio associated with being LTFU as a function of travel  
165 distance. We dichotomized travel distance to care at 8km based on Malawi's definition of access to care  
166 [26] and treated it as a time-varying covariate to control for length-biased sampling, i.e. that patients  
167 closer to care were often enrolled for longer periods of time [27,28]. We estimated unadjusted odds  
168 ratios and odds ratios adjusted for potential confounders, all of which remained constant over time.  
169 Statistical analyses were performed in R 3.1.0.

#### 170 *Ethics statement*

171 The Partners Healthcare Human Research Committee, USA (Protocol #: 2014P001460) and the  
172 National Health Sciences Research Committee of Malawi (Protocol #: 1216) granted ethical approval for  
173 this study.

#### 174 **Results**

175 Overall, 5,969 unique patients enrolled into ART care at a Neno District health facility between  
176 August 1, 2006 and November 1, 2012, and attended at least 2 visits. Of these patients, 351 (5.0%) were  
177 missing valid village information and 753 (12.6%) reported home villages outside of Neno District.  
178 Therefore, 4,865 unique patients (81.5%) ever enrolled in the ART program on or before November 1,  
179 2012 with at least 2 visits, 1,074 (22.1%) of whom transferred from one health facility to another at least  
180 once during the study period.

#### 181 *Phase Analysis*

182 Active patient enrollment increased from 537 patients at the end of phase 1 to 3,951 patients at  
183 the end phase 5 (Table 1, Figure 2). During phases 3 and 4, as additional ART facilities opened, most  
184 patients new to these facilities were new ART enrollees. However, 10% of patients transferred during

185 phase 3 (n/N= 221/2,293) and 23% (n/N= 842/3,591) in phase 4. During phase 5 with decentralization  
 186 complete, the percentage of transfers decreased to 2% (n/N= 86/3,951).

187 **Table 1. Demographic, clinical, and distance-to-care for patient cohorts during each phase of full**  
 188 **decentralization**

		Phase 1	Phase 2	Phase 3	Phase 4	Phase 5
	<b>Start of phase</b>	<b>1-Aug-06</b>	<b>1-Jun-08</b>	<b>1-Feb-09</b>	<b>1-Aug-10</b>	<b>1-May-12</b>
	<b>End of phase</b>	<b>31-May-08</b>	<b>31-Jan-09</b>	<b>31-Jul-10</b>	<b>30-Apr-12</b>	<b>31-Oct-12</b>
<i>Demographic information</i>						
	Health facilities providing ART	1	2	6	12	12
	Number of patients ever enrolled during phase	574	1103	2575	4072	4194
	Number of patients at end of phase <sup>1</sup> (%)	537 (94)	1035 (94)	2293 (89)	3591 (88)	3951 (94)
	Women (%)	361 (67)	677 (65)	1498 (65)	2406 (66)	2653 (67)
	Mean age at ART initiation (sd)	32.5 (13.9)	32.6 (14.1)	33.1 (14.4)	32.9 (13.8)	33.1 (13.8)
	Number of transfers during phase (%) <sup>2</sup>	0 (0)	3 (<1)	221 (10)***	842 (23)***	86 (2)***
<i>Clinical information</i>						
	Patients who started ART at WHO stage 3 or 4 (%) <sup>3</sup>	391 (73)	659 (64)***	1238 (54)***	1638 (46)***	1769 (45)***
	Median clinic visits per patient per year (IQR)	6.2 (5 to 7)	6.1 (5 to 7)	6.5 (6 to 8)***	7.3 (6 to 9)***	7.7 (6 to 9)***
	Patients with < 4 clinic visits per year (%)	27 (5)	67 (6)	109 (4)	32 (1)***	30 (1)***
	1-year retention of new patients enrolled during phase (%) <sup>4</sup>	491 (86)	453 (81)*	1234 (82)	1443 (84)	404 (82)
<i>Distance</i>						
	Mean travel distance to facility in km (sd) <sup>5</sup>	7.3 (5.4)	7.4 (5.3)	6.3 (4.2)***	4.7 (4.1)***	4.7 (4.2)***
	Patients greater than 8 km (Euclidian) (%)	260 (48)	516 (50)	884 (39)***	734 (20)***	792 (20)***
	Patients attending closest health facility (%) <sup>6</sup>	537 (100)	1008 (97)***	1935 (84)***	2785 (78)***	3080 (78)***
	Mean cost travel distance in km (sd) <sup>7</sup>	18.7 (15.7)	16.2 (15.7)**	10.9 (11.9)***	7.8 (9.5)***	7.9 (9.7)***

189  
 190 \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ ; all comparisons made to Phase 1

191 <sup>1</sup> Patients from Neno District enrolled in care at end of phase. All estimates exclude patients receiving care at Neno  
 192 facilities, but residing outside of Neno District.

193 <sup>2</sup> Patients who transferred from one Neno District clinic health facility to another Neno District clinic health facility  
 194 during phase. The denominator was number of patients ever enrolled during phase.

195 <sup>3</sup> 19% of observations were missing WHO stage at ART initiation.

196 <sup>4</sup> 1-year retention of all patients who first enrolled at any Neno health facility during the phase.

197 <sup>5</sup> Mean Euclidean distance from patient's home village to health facility where ART care was received. (km)

198 <sup>6</sup> A patient attended the nearest the health facility if she was enrolled at the facility that was the minimum  
199 Euclidean distance from the center of her home village.

200 <sup>7</sup> Mean cost distance from patient's home village to health facility where ART care was received (km)

201

202 **Fig 2. Map of decentralization of ART services from 2008 to 2012.**

203 Crosses show location of health facilities. Dots show number of ART patients by home village, color-  
204 coded by health facility patient attended. Larger dots indicate a larger number of patients.

205 Mean patient age at ART initiation was 33 years, and approximately two-thirds (64%) of patients  
206 were female. There was no evidence that age at initiation or patient gender varied by phase ( $p > 0.1$  for  
207 all comparisons). Over time, greater proportions of patients initiated ART for less clinically advanced HIV  
208 disease; the percentage of patients who had initiated ART at WHO stage 3 or 4 decreased from 73% in  
209 phase 1 to 45% in phase 5 ( $p < .001$ ).

210 At the end of phase 1, patients lived an average of 7.3 km from their ART facility, and 52% of  
211 patients lived beyond 8 km of their ART facility, not meeting the Malawi MOH's definition of access to a  
212 health facility [26] (Table 1). This percentage decreased significantly over time to 39% at the end of  
213 phase 3 ( $p < 0.001$ ) and 20% at the end of phase 5 ( $p < 0.001$ ), as average distance to the ART clinic  
214 decreased to 4.7 km ( $p < 0.001$ ). Mean cost distance to ART clinic, which considered topography in the  
215 distance calculation, decreased from 18.7 km at the end of phase 1 to 7.9 km at the end of phase 5 ( $p <$   
216  $0.001$ ). The proportion of patients with fewer than 4 visits per year ranged from 6% in phase 2 to 1% in  
217 phases 4 and 5. Overall, 85% of patients were retained in care for at least one year with minimal  
218 variability across phases.

219 *Transfer Analysis*

220 One thousand seventy-four patients transferred ART facilities at least once (Table 2). Sixty-eight  
221 percent ( $n/N=731/1,074$ ) of transfers were women. Mean travel distance decreased from 9.5  
222 kilometers to the patient's pre-transfer facility to 4.7 kilometers for her final facility ( $p < 0.001$ ), and the  
223 percentage of individuals living within 8 km of their health facility increased from 30% to 81% ( $p <$

224 0.001). Moreover, the proportion of individuals with <4 visits per year decreased from 11% for the  
 225 initial facility to 1% for the post-transfer facility ( $p < .001$ ).

226 **Table 2. Comparison of demographic, clinical and distance data for transfers and non-transfers**

		Transfers <sup>1</sup>		Non-Transfers <sup>2</sup>
		First Facility	Final Facility	Facility
<i>Demographic information</i>				
	Number of patients	1074	1074	3791
	Women (%)	731 (68)	731 (68)	2359 (62)***
	Mean age at ART initiation (sd)	31.8 (14.5)	31.8 (14.6)	33.6 (13.9)***
<i>Clinical information</i>				
	Patients starting ART at WHO stage 3 or 4 (%) <sup>3</sup>	557 (52)	557 (52)	1235 (33)***
	Median clinic visits per year (IQR)	6.7 (5.1 - 9.2)	6.6 (5.8 - 8.3)	8.3 (6.7 - 10.5)***
	Patients with <4 visits per year (%)	123 (11)	11 (1)***	45 (1)*
	LTFU at 1 year <sup>4</sup>	19 (0.02)	19 (0.02)	652 (0.17)***
<i>Distance</i>				
	Mean travel distance to facility, km (sd) <sup>5</sup>	9.5 (4.6)	4.7 (4.4)***	5.1 (4.5)**
	Patients within 8 km (Euclidean) (%)	322 (3)	874 (81)***	2868 (76)**
	Mean cost travel distance in km (sd) <sup>6</sup>	19.7 (16.8)	9.6 (11.4)***	8.4 (1.8)**

227

228 \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$

229 <sup>1</sup> Comparisons are between differences between transfers at their first facility, compared to the same patients  
 230 while receiving ART at their final facility (repeated-measures ANOVA/Wilcox test for medians)

231 <sup>2</sup> Compares patients who never transferred (non-transfers) to transfers at final facility (ANOVA/Wilcox test for  
 232 medians)

233 <sup>3</sup> Data were missing for 292 transfers at first facility, 229 transfers at final facility, and 1234 non-transfers.

234 <sup>4</sup> Patients alive and in care at any Neno health facility one year after enrollment

235 <sup>5</sup> Mean Euclidean distance from patient's home village to health facility where ART care was received (km)

236 <sup>6</sup> Mean cost distance from patient's home village to health facility where ART care was received (km)

237

238 We also compared patients who experienced at least one transfer (i.e. "transfers") to those who

239 were only enrolled at one facility during their time in care (i.e. "non-transfers") (Table 2). Patients who

240 transferred tended to have more severe disease (52% with WHO stage 3 or 4 versus 33% in non-

241 transfers). Only 45 (1.2%) of non-transfer patients had <4 visits per year, similar to transfer patients at

242 their final facility, 1.0% per year ( $p = 0.08$ ). Non-transfers traveled a mean of 5.1 km, similar to the

243 average of 4.7 km traveled by transfers to their final facility. Non-transfer patients were more likely to  
 244 be LTFU at 1 year (17%) than transfer patients (2%;  $p < 0.001$ ).

245 *Distance Analysis*

246 In our univariate analysis ( $n=4,865$ ), the hazard ratio associated with living  $>8$  km from a health  
 247 facility compared to  $\leq 8$  km from a health facility was 1.7 (95% CI: 1.5–1.9) (Table 3). In multivariate  
 248 analysis (Table 3) that controlled for possible confounders, including gender, age, and transfer status,  
 249 the hazard ratio was slightly larger (aHR = 2.0, 95% CI: 1.8–2.3). Including WHO stage at ART initiation ( $n$   
 250 = 3,462) did not substantially change the estimate of the effect of travel distance on LTFU (aOR = 1.9,  
 251 95% CI: 1.7-2.2).

252 **Table 3. Association between travel distance to care and hazard of loss to follow up (LTFU), and**  
 253 **exploratory analysis of association between patient covariates and LTFU.**  
 254 *Cox proportional hazards regression ( $n = 4,865$ ): primary outcome variable was loss to follow up. Travel*  
 255 *distance was treated as a time-varying covariate; other covariates remained constant over time.*  
 256

		Unadjusted OR (95% CI)	Adjusted OR (95% CI) <sup>1</sup>
<i>Travel distance</i> <sup>2</sup>			
	< 8 km	1.00 (Ref)	1.00 (Ref)
	$\geq 8$ km	1.70 (1.51-1.91)***	2.04 (1.81-2.30)***
<i>Age (years)</i> <sup>3</sup>		1.00 (1.00-1.01)	1.00 (0.99-1.00)
<i>Gender</i>			
	Female	1.00 (Ref)	1.00 (Ref)
	Male	1.64 (1.46-1.84)***	1.55 (1.38-1.74)***
<i>Transfer</i> <sup>4</sup>			
	No	1.00 (Ref)	1.00 (Ref)
	Yes	0.37 (0.31-0.45)***	0.32 (0.27-0.38)***

257  
 258 \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$

259 <sup>1</sup> Adjusted for all other variables in table

260 <sup>2</sup> Euclidean distance from patient’s home village to health facility where ART care was received; measured as a time-varying  
 261 covariate based on a patient’s location during a particular time interval

262 <sup>3</sup> Age at ART initiation, centered at mean

263 <sup>4</sup> Compares patients who transferred from one Neno health facility to another at least once to those who remained enrolled at  
 264 the same health facility.

265  
 266  
 267

268 **Discussion**

269       Employing the first application of geospatial data, to our knowledge, to quantify the relationship  
270 between patient-level travel distance to ART services and patient outcomes, we examined the impact of  
271 ART decentralization on travel distance, appointment adherence, and LTFU in a rural setting in SSA. We  
272 observed that ART decentralization was associated with increased patient enrollment, reduced patient  
273 travel distance, and decreased LTFU.

274       Though HIV testing and counselling (HTC) was available at all Neno health facilities beginning in mid-  
275 2007, many patients testing positive for HIV and meeting ART criteria did not begin ART until their local  
276 facility offered it. By 2012, when ART was available at all 12 facilities in the district, the home village  
277 distribution of ART patients corresponded roughly to the general population distribution, as compared  
278 to the patient home village distribution in 2008, which was highly concentrated around the only facility  
279 then offering ART. By the end of the 2012, 80% of patients in Neno traveled less than 8 km to reach their  
280 chosen facility, a marked increase from mid-2008 when ART was only available at the district hospital.  
281 Furthermore, among patients who transferred to a closer facility after having previously received ART at  
282 another facility located further away, the percentage with poor appointment adherence decreased from  
283 11% to 1% after transfer. Proximity to ART care appeared to be a key driver for treatment initiation and  
284 adherence in this rural African population with little access to motorized transportation.

285       Previous studies from Malawi have demonstrated conflicting results about the effects of ART  
286 decentralization on patient outcomes. In rural Thyolo District, although the incidence of patient LTFU  
287 was significantly lower for patients started on ART at primary health facilities compared to those  
288 initiating ART at the district hospital, ART decentralization was associated with higher patient mortality  
289 [11]. In Zomba District, patients receiving decentralized care were 40% less likely to experience LTFU  
290 and death during the 10 month study period but the study included a relatively healthy population [29].

291 Our results suggest that full ART decentralization for all patients can achieve favorable results in Malawi  
292 and similar impoverished rural SSA regions and may help achieve the ART and viral suppression targets  
293 of the 90-90-90 UNAIDS targets.

294 We detected a difference in LTFU between ART enrollees who transferred facilities, often enrolling  
295 in earlier phases, and later enrollees who initiated ART once a nearby facility began offering treatment.  
296 Eighty-three percent of patients who did not transfer were retained in care for at least 1 year, compared  
297 to 98% of transfers, despite similar average travel distances. We hypothesize that patients who enrolled  
298 in ART earlier, when ART facilities were more limited, were generally a more adherent population.  
299 Particularly for non-transfers, who often enrolled in care later, travel distance was strongly associated  
300 with LTFU.

301 The major strength of this study resides in our ability to examine the longitudinal relationship  
302 between individual patients' distance to care and ART treatment outcomes. Previous research has  
303 typically divided patients into those receiving care at centralized facilities and those receiving care at  
304 decentralized facilities, without the ability to detect patient-level variations in travel time [6,29,30].  
305 While some studies have investigated travel time for HIV patients [31,32], these either did not examine  
306 patient outcomes, or found little relationship between travel time and appointment adherence. By  
307 contrast, we observed a strong association between distance to care and LTFU.

308 Our study had several limitations. First, guideline changes and other secular trends during the study  
309 period may have introduced bias. For example, in 2011, the Option B+ strategy was introduced  
310 nationally resulting in increased ART enrolment of relatively healthy individuals. In addition, anecdotal  
311 evidence suggests that HTC uptake increased in Neno as ART initiation services became available in new  
312 facilities. As a result, the number of patients eligible to begin ART significantly increased over time, and  
313 we were unable to disentangle how decentralized care affected ART enrollment after accounting for

314 these factors. Second, missing clinical information, such as baseline WHO stage, limited our ability to  
315 track changes in our cohort over time, particularly with regard to HIV disease severity and  
316 immunosuppression at ART initiation. Third, because Malawi lacks data on subnational HIV trends [33],  
317 we were unable to consider ecological trends in HIV prevalence in Neno.

318 Our geospatial analysis also had some limitations. As each village had only one GPS point, we could  
319 only approximate each patient's home location, and because the electronic medical record did not  
320 always denote patient address changes, we were unable to detect all patient moves. Village data was  
321 also missing for approximately 5% of patients. Euclidean distances do not represent the true distance a  
322 patient travels to receive care given that footpaths and roads adapt to terrain. The use of cost distance  
323 corrects for elevation changes, but likely still underestimates the true distance traveled by patients to  
324 reach their health facility. Finally, we were unable to identify patients who initiated and maintained ART  
325 at mobile clinics prior to the opening of the nearest decentralized ART clinic, which may have  
326 overestimated travel distance.

327 Nevertheless, we believe that the results of our study are generalizable to other rural settings in  
328 Malawi and elsewhere in SSA. We observed a strong association between ART decentralization,  
329 decreased patient travel distance, and increased ART enrollment and retention in care. Our data,  
330 derived from a governmental ART program, reflect that full ART decentralization can improve treatment  
331 outcomes even under "real-world" clinical conditions in an extremely impoverished, rural district. The  
332 use of GIS technology and mathematical modeling can further support the rational and equitable  
333 introduction of additional ART sites in Malawi [34]. As care for other chronic illnesses is scaled up and  
334 decentralized in SSA, it will be useful to assess geographic access to care and its relationship to  
335 treatment adherence and other disease outcomes.



336 In conclusion, our findings highlight the benefits of decentralized ART care and the potential of  
337 increasingly robust geographic information systems to improve our understanding of how distance to  
338 health facilities affects LTFU and other outcomes for HIV-infected patients.

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