

1 **Retention and predictors of attrition among patients who started antiretroviral therapy**
2 **in Zimbabwe's National Antiretroviral Therapy Programme between 2012 and 2015**

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19

20 **Abstract**

21 **Background**

22 The last evaluation to assess outcomes for patients receiving antiretroviral therapy (ART)
23 through the Zimbabwe public sector was conducted in 2011, covering the 2007-2010 cohorts.
24 The reported retention at 6, 12, 24 and 36 months were 90.7%, 78.1%, 68.8% and 64.4%,
25 respectively. We report findings of a follow up evaluation for the 2012-2015 cohorts to assess
26 the implementation & impact of recommendations from this prior evaluation.

27 **Methods**

28 A nationwide retrospective study was conducted in 2016. Multi-stage proportional sampling
29 was used to select health facilities and study participants records. The data extracted from
30 patient manual records included demographic, baseline clinical characteristics and patient
31 outcomes (active on treatment, died, transferred out, stopped ART and lost to follow-up
32 (LFTU)) at 6, 12, 24 and 36 months. The data were analysed using Stata/IC 14.2. Retention
33 was estimated using survival analysis. The predictors associated with attrition were determined
34 using a multivariate Cox regression model.

35 **Results**

36 A total of 3,810 participants were recruited in the study. The median age in years was 35 (IQR:
37 28-42). Overall, retention increased to 92.4%, 86.5%, 79.2% and 74.4% at 6, 12, 24 and 36
38 months respectively. LFTU accounted for 98% of attrition. Being an adolescent or a young
39 adult (aHR 1.41; 95%CI:1.14-1.74), receiving care at primary health care facility (aHR 1.23;
40 95%CI:1.01-1.49), having initiated ART between 2014-2015 (aHR 1.45; 95%CI:1.24-1.69),
41 having WHO Stage 4 (aHR 2.06; 95%CI:1.51-2.81) and impaired functional status (aHR 1.24;
42 95%CI:1.04-1.49) predicted attrition.

44 **Conclusion**

45 The overall retention was higher in comparison to the previous 2007–2010 evaluation. Further
46 studies to understand why attrition was found to be higher at primary health care facilities are
47 warranted. Implementation of strategies for managing patients with advanced HIV disease,
48 differentiated care for adolescents and young adults and tracking of LFTU should be prioritised
49 to further improve retention.

50

51 **Key words**

52 ART outcomes, implementation, low resource setting, differentiated care, Zimbabwe

53

54

55 **Introduction**

56 Globally by the end of 2018, there were 37.9 million [32.7 million–44.0 million] people living
57 with HIV (PLHIV) with 61% of these residing in Eastern and Southern Africa (ESA) [1]. Over
58 the past two to three decades, investments in the global HIV response have achieved
59 unprecedented results with the number of new HIV infections significantly reduced from 2.9
60 million [2.3 million–3.8 million] in 1997 to 1.7 million [1.6 million–2.3 million] new infections
61 by 2018 and 23.3 million PLHIV put on treatment globally [1]. Between 2010 and 2018 new
62 HIV infections and deaths decreased by 16% and 33%, respectively [2]. Despite these
63 remarkable achievements, patient attrition and losses to follow-up (LTFU) still remain
64 legitimate threats to the long-term success of antiretroviral therapy (ART) scale up [3].

65

66 PLHIV on ART who are not retained in care are at increased risk of developing drug resistance
67 and dying [4]. Based on a systematic review of several studies that have been conducted in low
68 resource settings, key predictors of high attrition include patients with advanced HIV-disease
69 progression [marked by body mass index (BMI) <18 kg/m², baseline CD4 counts <200
70 cells/mL, World Health Organisation (WHO) Stage - III and IV, poorer level of functionality],
71 male sex, younger age and having lower levels of education [5]. Early ART initiation as
72 measured by shorter time duration between HIV testing and ART initiation has been shown to
73 reduce risk of attrition[6,7]. Other studies have however shown that those who initiate ART at
74 a higher baseline CD4 may also be prone to attrition [8,9].

75

76 Numerous studies assessed attrition and the effect of different initiatives on treatment outcomes
77 at selected health facilities in resource-limited settings [7,8,10–12]. They mainly reflect the
78 experience of academic, standalone, donor supported or private institutions that generally have
79 better data collection systems, are well financed and have better human resources for health,

80 which may not be generalizable. In scenarios where outcomes for routine programmes have
81 been reported, evaluations have often been regional, limited to a few facilities or targeting only
82 a specific subpopulation of the HIV cohorts (children, adolescents or adults) [6,13–17]. There
83 is paucity of data demonstrating treatment outcomes and impact of ART at a national level in
84 many resource-limited settings. Periodic national treatment outcome evaluations provide
85 information needed for targeted interventions that will allow national HIV programmes to
86 achieve the ambitious UNAIDS 3rd 90 by 2020.

87

88 Zimbabwe started rolling out ART in the public health system in 2004 in 5 pilot facilities. Since
89 then, there has been significant scale-up with more than 1500 health institutions offering ART
90 by the end of 2017 [18]. This rapid scale-up has been mostly attributed to the rapid adaptation
91 of the WHO HIV guidelines and the widespread decentralization of comprehensive HIV
92 services which was supported by health care worker task-shifting policies and significant
93 investments in training, supportive supervision and clinical mentoring [19]. Funding from the
94 Government of Zimbabwe, Global Fund for AIDS, Tuberculosis, and Malaria (GFATM), the
95 United States of America President's Emergency Plan for AIDS Relief (PEPFAR) and other
96 donors supported the scale-up the program.

97

98 An evaluation of the Zimbabwe national ART programme, which only included adults (> 15
99 years) living with HIV started on ART between 2007-2010, reported 90.7%, 78.1%, 68.8% and
100 64.4% retention at 6, 12, 24 and 36 months, respectively [17]. These findings mirrored
101 treatment outcomes in other parts of sub-Saharan Africa and recommendations given included
102 strengthening earlier diagnosis and linkages to treatment; further decentralization of
103 comprehensive HIV services to improve ART coverage and adaptation of innovative strategies

104 aiming at improving patient retention (adherence clubs, food supplementation and mobile short
105 messages service (SMS) reminders) [17].

106 In our study, we report results of a 2016 follow-up evaluation of treatment outcomes of the
107 Zimbabwe National ART Programme, conducted among individuals who started ART between
108 2012-2015, prior to the implementation of the HIV ‘Treat All’ policy. This nationwide follow-
109 up evaluation therefore assessed the impact of the interventions implemented since the first
110 evaluation. The assessment was expanded to include children and adolescents and was aiming
111 to determine retention and estimate risk factors associated with attrition among the different
112 population target groups.

113

114 **Material & Methods**

115 **Study design**

116 A retrospective cohort analysis was undertaken among children, adolescents and adults living
117 with HIV who started ART in Zimbabwe between October 2012 and January 2015.

118

119 **Study setting**

120 The study was conducted at selected public health institutions across all the country's 10
121 provinces. Zimbabwe has a population of around 13 million [20]. The country has a generalised
122 HIV epidemic and prevalence has continued to hover between 13 % and 16 % for the past
123 decade. Currently there are about 1.4 million PLHIV of which 1.0 million (71%) were on
124 (ART) by December 2018 [18]. Since 2004 the country has adopted all the successive changes
125 in the WHO recommendations to start ART. Patients were eligible to start ART when they had
126 a CD4 count <350 cells/mL in 2010, CD4 <500 cells/mL in 2013 and since 2016, patients are
127 eligible regardless of their CD4 count (Treat All). The country has made significant progress
128 towards achieving the 90-90-90 targets. In a recent survey, 74.2% reported knowing their HIV
129 status; 86.8% self-reported current use of ART and among those who self-reported current use
130 of ART, 86.5 % were virally suppressed [21].

131

132 During the period between 2011 and 2015, the Zimbabwe National AIDS Strategic Plan II
133 (ZNASP-II) 2011-15 was developed to guide the scale-up of HIV care and treatment services
134 towards universal access [22]. In 2013, the country adopted the 2013 WHO guidelines which
135 recommended the CD4 < 500 cells/mL threshold for ART initiation. A 'test and treat' approach
136 was adopted for all HIV-positive children under 5 years, TB/HIV co-infected, HBV/HIV co-
137 infected, the HIV-positive partner in HIV sero-discordant relationship and pregnant and

138 breastfeeding mothers (Option B+). The preferred first-line regimen for adults, adolescents,
139 and older children was changed from stavudine, lamivudine and nevirapine (d4T/3TC/NVP)
140 to a once-daily pill of tenofovir, lamivudine and efavirenz (TDF/3TC/EFV) with zidovudine
141 and nevirapine as alternatives for TDF and EFV respectively. After ART initiation stable
142 patients were reviewed every 3 months and drugs were dispensed directly from the health
143 facilities. Monitoring was mainly clinical (weight, WHO clinical stage and assessment of
144 opportunistic infections) at every visit, complemented with laboratory tests (CD4 testing) every
145 6 months. Compared to the previous period access to CD4 testing improved significantly. By
146 the end of 2015, laboratory based CD4 testing was available in each of the 63 districts as
147 compared to 47 in 2009 [23]. On top of laboratory based CD4 testing, more than 265 point of
148 care (POC) CD4 testing devices were procured and distributed throughout the country mainly
149 to support the roll out of Option B+ [24]. Blood collection and transportation systems were put
150 in place to support facilities without access to CD4 testing. Routine viral load testing was not
151 available in the public sector and there was limited access to targeted viral load testing for
152 patients with suspected treatment failure. The monitoring and evaluation system was mainly
153 paper based. A few high-volume facilities started to implement an electronic patient monitoring
154 system (ePMS) which operated concurrently with the usual paper-based system.

155

156 **Sample size and sampling criteria**

157 A minimum sample of 4000 patient charts was required to estimate 12-month ART retention
158 (the outcome of interest), after assuming: 50% ART retention at 12 months after initiation, 20%
159 of charts would be missing, a margin of error of 5% and a design effect of 2.0. For logistical
160 and financially feasibility purposes, sampling was restricted to 1,389 ART sites across all 10
161 provinces that were supporting ≥ 50 HIV-positive clients on ART for at least 12 months by
162 January 2016. The sites were stratified into seven strata according to their patient volumes

163 receiving ART care and ordered by province and district within each stratum. From these, 70
164 (5%) ART sites were sampled using a probability proportional to size sampling criteria based
165 on client volumes receiving ART at each site. At the sampled sites, a line-listing was generated
166 in Excel for all HIV positive children, adolescents, adults and pregnant women initiated on
167 ART at the sampled sites between 1 October 2012 and 31 January 2015 using their unique ART
168 numbers obtained from the facility ART register. Following this, the required number of patient
169 ART care booklets were randomly selected without replacement according to their stratum
170 based on random schedule generator in Stata. If a selected ART care booklet was not traceable,
171 the next record was traced until the required sample size by site was reached

172

173

174 **Study variables and treatment outcomes**

175 The data collected included demographics (age, sex and marital status), clinical and
176 programmatic variables. Baseline clinical parameters collected at point of ART initiation
177 included WHO stage, functional status and pregnancy. Programmatic data collected included
178 level of care, date of HIV testing, date of enrolment and date of ART initiation. Date of last
179 clinic visit, date of next scheduled clinic visit and date of transfer-out/death/stopping ART were
180 also collected and used determine ART outcomes (i.e. active on treatment, LTFU, dead,
181 transferred out and stopped ART). The date the patient outcome was ascertained was also
182 collected. Patients were considered LTFU if they were more than 180 days without visit at the
183 clinic on the date of data abstraction.

184

185 **Data Collection Procedures**

186 Ten teams of three data abstractors collected the data using a structured tool. The data

187 abstractors underwent a 5-day training programme to acquaint them with study tools and study
188 procedures. Data collection tools were piloted to identify weaknesses which then were
189 rectified. The primary source document for the study was the patient manual medical records
190 (Patient OI/ART Booklets) being kept at the health institution. Other sources to complement
191 or validate the information included the different registers and interviews with at least one
192 experienced health care worker at each sampled site. Data was collected using Open Data Kit
193 (ODK) software on Android devices. Data was downloaded at regular intervals for cleaning,
194 quality control checks, merging and backing up. Data from a sample of 10% of the selected
195 charts was re-abstracted as a quality control check measure. Discrepancies were addressed by
196 both the team leader and data abstractors.

197

198 **Data Analysis**

199 The data were analysed using Stata/IC 14.2 [25]. The primary outcome was attrition, and this
200 was defined as either being dead, LTFU or stopped ART. A Cox proportional hazard model
201 was used to compute crude and adjusted hazard ratios and their 95% confidence intervals
202 estimating the association between explanatory variables and attrition. Time to attrition was
203 calculated as the time between the date of ART initiation and the date of outcome or last patient
204 clinic visit. Those active on ART and transferred out were censored on the date of data
205 abstraction and the date they were transferred out. Kaplan–Meier techniques were used to
206 estimate retention on ART at 6, 12, 24 and 36 months. The retention at 6, 12, 24 and 36 months
207 for adults (> 15years) was compared with the prior evaluation and two-sample test of
208 proportions was used to assess if there was a difference. The log rank test was used to assess if
209 differences between survival curves were statistically significant. A hierarchical approach was
210 employed where all variables associated with P-value <0.1 in the univariable were included

211 initially in the multivariable model. A stepwise backward elimination until all remaining
212 variables were significantly associated with attrition (p-value < 0.05).

213

214 **Ethical Considerations**

215 The evaluation protocol received ethics approval from Medical Research Council of Zimbabwe
216 (MRCZ/A/2033). The protocol was also sanctioned by the MoHCC. Confidentiality and
217 anonymity of ART clients was protected use their unique ART numbers as no names were
218 abstracted. Permission to conduct the evaluation was sought at various levels of the tiered
219 health delivery system. All data abstractors signed confidentiality forms.

220

221 **Results**

222

223 A total of 3,993 (99.8%) records were abstracted out of a target of 4,000. On data cleaning
224 3,810 (95.4%) records were found to be of quality standard for the analysis (Fig 1)

225

226 **Fig 1. Study Population**

227 Of 3,810 patients included, 38.7% and 48.6% started ART in 2013 and 2014, respectively, and
228 59.4% were female. The median age in years was 35 [interquartile range (IQR):28-42]. Most
229 patients were adults (71.8 %), married (55.8%), and had a normal functional status (73.4%).
230 Few (3.1%) were in WHO stage IV, and 27.1% started ART at a primary health care (PHC)
231 facility. Among women of child bearing age 10.4% reported to be pregnant at time of ART
232 initiation, 5.5% of the total study population (Table1).

233

234 **Table 1. Baseline characteristics of 3810 patients who started ART between 2012-2015,
235 in Zimbabwe**

	N	(%)
Total	3810	100.0
Year of ART initiation		
2012	289	(7.6)
2013	1476	(38.7)
2014	1850	(48.6)
2015	195	(5.1)
Sex		
Female	2262	(59.4)
Male	1548	(40.6)
Median Age (N=3700) (IQR)		
Age groups		
Children (0-15 years)	254	(6.7)
Adolescents & young adults (15-24years)	385	(10.1)
Adults (25-49 years)	2735	(71.8)
Elderly (>=50 years)	424	(11.1)
Missing	12	(0.3)
Pregnancy at ART initiation		
Confirmed	208	(5.5)
Not confirmed	3602	(94.5)
Marital status of patient		
Single & divorced	863	(22.7)
Married	2125	(55.8)
Widowed	434	(11.4)

N/A Child	318	(8.3)
Missing	70	(1.8)
Baseline Functional Status		
Impaired	811	(21.3)
Normal	2796	(73.4)
Missing	203	(5.3)
Baseline WHO Stage		
WHO Stage I	821	(21.5)
WHO Stage II	1245	(32.7)
WHO Stage III	1447	(38.0)
WHO Stage IV	120	(3.1)
Unknown	177	(4.6)
Level of Care		
Central Hospital	888	(23.3)
Provincial Hospital	341	(9.0)
Mission/District Hospitals	1549	(40.7)
Primary Health Care facilities	1032	(27.1)

N - Number of observations, ART - Antiretroviral Therapy,
IQR - Interquartile Range, N/A - Not applicable, WHO -
World Health Organisation,

236

237 Fig 2 shows that the proportion of patients receiving ART at PHC facilities increased gradually
238 from 21.6% in 2012 to 34.5% in 2015.

239

240 **Fig 2. Level of care where the 3,810 patients started ART between 2012-2015, in**
241 **Zimbabwe**

242

243 Fig 3 shows that retention was significantly lower among patients who started ART between
244 2014-2015 as compared to those who started between 2012-2013 period (log-rank test:
245 $p<0,001$).

246

247 **Fig 3. Comparison of retention rates of 3,810 patients who started antiretroviral therapy**
248 **between 2012-2013 and 2014-2015 in Zimbabwe**

249 Overall, retention at 6, 12, 24 and 36 months was 92.4%, 86.5%, 79.2% and 74.4%, respectively. Table 2 shows a comparison between adult
 250 patients who started ART between 2007-2010 and 2012-2015. Retention at 6, 12, 24 and 36 months was 1.4%, 10.0%, 14.3% and 14.5% higher
 251 among patients who started between 2012-2015. Differences were statistically significant except at 6 months.

252 **Table 2. Retention in care of patients who started antiretroviral therapy between 2007-2010 and 2012-2015 in Zimbabwe**

	Months since ART initiation	2012-2015 Evaluation			2007-2010 Evaluation			Difference		
		N	Retention (%)	95% CI	N	Retention (%)	95% CI	%	95%CI	^a P value
Overall	6	3476	92.4	(91.5 – 93.2)						
	12	3066	86.5	(85.3 – 87.5)						
	24	1427	79.2	(77.7 – 80.6)						
	36	222	74.4	(72.5 – 76.1)						
Children < 15 years	6	250	97.3	(94.4 – 98.7)						
	12	230	94.2	(90.5 – 96.4)						
	24	114	86.3	(81.0 – 90.2)						
	36	17	82.3	(75.5 – 87.4)						
Adults > 15 years	6	3222	92.0	(91.1 – 92.9)	3739	90.7	(86.1 – 93.8)	1.4	(-0.02 – 2.6)	0.06
	12	2832	85.9	(84.7 – 87.0)	3641	78.1	(67.7 – 84.7)	10.0	(5.9 – 10.0)	<0.001
	24	1311	78.7	(77.1 – 80.1)	2003	68.8	(58.5 – 77.5)	14.3	(6.9 – 12.9)	<0.001
	36	204	73.7	(71.8 – 75.6)	806	64.4	(55.7 – 72.3)	14.5	(2.4 – 16.2)	<0.001

^aTwo-sample test of proportions

253

254

255

256

257 Over 6,508 years of patient follow up; 77.4% were active on treatment, 2.4% transferred out and 20.2% were lost through attrition (LTFU 19.8 %,
 258 and died 0.4%) The median follow-up time per patient was 1.7 years IQR (1.1-2.4). The overall attrition rate was 11.8, [95% confidence interval
 259 (CI):11.0-12.7] per 100 person years (PY). The other attrition rates are shown in Table 3.

260 **Table 3. Bivariate and multivariate analysis of factors associated with attrition in the 2012-2015 ART cohort**

Variable	Categories	Total	PT years	Attrition ^{\$}	Attrition %	Attrition Per 100PY	HR	p	95%CI	aHR	P	95%CI
Total		3810	6508	768	20.2	11.8						
Sex	Female	2262	3793	440	19.5	11.6	1					
	Male	1548	2689	328	21.2	12.2	1.06	0.4	(0.92 - 1.23)	NS	NS	
Age group	Adults	2735	4664	555	20.3	11.9	1			1		
	Children	254	467	35	13.8	7.5	0.62	0.006	(0.44 - 0.87)	0.62	0.007	(0.44- 0.88)
	Adolescents & young adults	385	563	103	26.8	18.3	1.47	<0.001	(1.19 - 1.82)	1.41	0.002	(1.14 - 1.74)
	Elderly	424	781	75	17.7	9.6	0.81	0.1	(0.64 - 1.04)	0.83	0.1	(0.65 - 1.05)
	Missing	12		0	0.0	0.0						
Marital Status	Married	2125	3612	419	19.7	11.6	1					
	Single & divorced	863	1384	202	23.4	14.6	1.25	0.01	(1.05 - 1.47)			
	Widowed	434	773	85	19.6	11.0	0.97	0.8	(0.76 - 1.22)	NS	NS	
	Child N/A	318	583	49	15.4	8.4	0.74	0.4	(0.55 - 0.99)			
	Missing	70	133	13	18.6	9.8	0.88	0.6	(0.51 - 1.53)			
Level of Care	Central & province	1229	2110	230	18.7	10.9	1			1		
	Primary health care facility	1032	1664	213	20.6	12.8	1.15	0.1	(0.96 - 1.39)	1.23	0.04	(1.01 - 1.49)
	District	1549	2708	325	21.0	12.0	1.10	0.2	(0.93 - 1.31)	1.21	0.04	(1.01 - 1.44)
Year ART Initiation	2012-13	1765	4011	377	21.4	9.4	1			1		
	2014-2015	2045	2490	391	19.1	15.7	1.45	<0.001	(1.24 - 1.69)	1.45	<0.001	(1.24 - 1.69)
WHO Stage	I-III	3513	5921	675	19.2	11.4	1			1		
	IV	120	194	43	35.8	22.2	1.95	<0.001	(1.43 - 2.66)	2.06	<0.001	(1.51 - 2.81)
	Missing	177	350	50	28.2	14.3	1.34	0.05	(1.00 - 1.78)	1.52	0.04	(1.02 - 2.27)
Functional status	Normal	2796	4761	538	19.2	11.3	1			1		
	Impaired	811	1321	177	21.8	13.4	1.18	0.06	(0.99 - 1.40)	1.24	0.02	(1.04 - 1.49)
	Missing	203	396	53	26.1	13.4	1.26	0.1	(0.95 - 1.67)	1.01	0.9	(0.69 - 1.50)
Pregnant when starting ART	Not confirmed	3602	6243	718	19.9	11.5	1			NS	NS	
	Confirmed	208	270	50	24.0	18.5	1.48	0.007	(1.12 - 1.98)			

NS= Not significant; HR= Hazard Ratio; aHR=adjusted Hazard Ratio; CI= Confidence Interval; ART= Antiretroviral Therapy; WHO= World Health Organisation
 \$ either death or LTFU

262 On bivariate analysis, being an adolescent or a young adult [hazard ratio (HR) 1.47; 95%
263 CI:1.19-1.82], being single or divorced (HR 1.25; 95 CI:1.05-1.47), having initiated ART
264 between 2014-2015 (HR 1.45; 95% CI:1.24-1.69), having WHO Stage 4 (HR 1.95; 95%
265 CI:1.43-2.66) , and being pregnant at time of ART initiation (HR 1.48; 95% CI:1.12-1.98) were
266 associated with attrition (p<0.05). Risk of attrition among children (<15years) was 40% lower
267 as compared to adults. In addition, being elderly (HR 0.81; 95%CI:0.64-1.04) and receiving
268 care at PHC facility (HR 1.15; 95%CI:0.96-1.39) were associated at level 0.1 and included in
269 the multivariable regression model.

270

271 In multivariable analysis, being an adolescent or a young adult [multivariable-adjusted hazard
272 ratio (aHR)1.41; 95% CI:1.14-1.74], receiving care at PHC facility and district level (aHR 1.23;
273 95% CI:1.01-1.49) and (aHR 1.21; 95% CI:1.01-1.44), having initiated ART between 2014-
274 2015 (aHR 1.45; 95% CI:1.24-1.69), having WHO Stage 4 (aHR 2.06; 95% CI:1.51-2.81), and
275 having an impaired functional status (aHR1.24; 95% CI:1.04-1.49) were associated with
276 attrition (Table 3).

277

278

279 Discussion

280 This follow-up evaluation of the Zimbabwe National ART programme, which included
281 children, adolescents and adults started on ART between 2012 and 2015, showed an overall
282 improvement of the performance of the ART programme compared to those started on ART
283 between 2007-2010 [17]. Attrition was mainly explained LTFU. Retention observed in this
284 evaluation was above what is reported for children, adolescents and adults in other similar
285 studies from low resource settings [26–28]. Adolescents and young adults, patients with
286 advanced HIV disease (WHO Stage 4, impaired functional status), those receiving care at PHC
287 level and starting treatment after 2013, when the country switched treatment guidelines to the
288 500 CD4 cells/mL threshold, were at risk of attrition.

289

290 The increase in retention since the previous evaluation may be explained by strategies put in
291 place by the MoHCC. Relying on a vast body of evidence showing that decentralisation
292 increases access to ART and retention in care [29], the prior evaluation recommended further
293 decentralization. Moreover, other innovative strategies to improve patient retention, such as
294 adherence clubs, food supplementation and mobile short messages service (SMS) reminders
295 were recommended [17]. Our data show a substantial increase of the proportion of patients
296 receiving ART at PHC level. This decentralization was supported by policy shifts (in particular,
297 the provision for nurses to initiate ART in non-complicated cases), and by significant
298 investments in training, supportive supervision and clinical mentoring [30]. In addition to
299 decentralisation, the improvement in retention could also be attributed to adoption of WHO
300 guidance for earlier ART initiation among those tested HIV-positive with CD4<500 cells/mL
301 compared to the previous 350 cells/mL CD4 threshold. For instance in this cohort 41.1% had
302 WHO stage 3 or 4 compared to 87.6% in the previous study [17]. However, other recommended
303 measures, such as food supplementation, adherence clubs, mobile short messages service

304 (SMS) reminders, fast tracking of stable patients on ART, community and family ART refill
305 groups, were not implemented on a wide scale in the public sector.

306
307 However, the increase of decentralized ART does probably not explain the higher level of
308 retention, compared to the previous evaluation. Surprisingly, our study showed that receiving
309 ART at PHC level was associated with attrition. This finding contrasts with the findings of the
310 previous evaluation. In the previous evaluation, retention among patients receiving ART at
311 PHC level was better than among those initiating ART at higher levels of care, in particular
312 district/mission hospitals [17]. We speculate that the higher level of attrition in PHC facilities
313 may be explained by the massive decentralisation (down referral), which happened during the
314 current evaluation period, whereby patients who started ART at district/provincial hospitals
315 were referred to PHC level for follow-up. Implementation of policy changes may be abrupt and
316 have an adverse effect. After assessment by a healthcare worker, stable patients may have little
317 or no opportunity to object against the decision to be referred to another clinic. Patients referred
318 to a clinic which is not of their choice are more likely to self-transfer to another facility of their
319 choice. Such patients are then considered as LFTU in one clinic, while retained in another
320 clinic. Moreover, at the beginning of the decentralisation process, care at PHC level may not
321 have been fully developed. Another study showed that abrupt down-referral may lead to a
322 decrease in quality of care and resulting in worse health outcomes [31]. When PHC facilities
323 are ill prepared, usually outcome monitoring is poor. The country has almost completed the
324 decentralisation process for ART services and the focus now should be on improving the
325 quality of care at PHC facilities. The necessary health system support structures which include
326 human resources for health (recruitment, training and capacity building), drug supply,
327 monitoring and evaluation should be prioritised.

328

329 Most of the reported attrition (98%) was due to LFTU. This finding was similar to the prior
330 evaluation where LFTU also accounted for the larger proportion of attrition. Determining true
331 LTFU is not always easy. A recent meta-analysis showed that, of patients LTFU and traced,
332 30% had self-transferred, 30% had stopped taking ART and the other 30% had died [32]. We
333 therefore hypothesize that the increased LTFU in our study might be administrative, especially
334 at PHC level where monitoring is less well developed. A substantial proportion of patients may
335 seem LTFU, but be in care at another or even the same clinic with another identification number
336 [31]. The probability of administrative reasons for LTFU is probably higher at PHC facilities,
337 especially when paper-based tools are used to monitor and report treatment outcomes [31].
338 Poor documentation of clinic visits and transfers in medical records may result in
339 administrative LTFU. There is need to determine the true nature of the outcome of patients
340 LTFU within the Zimbabwe ART programme. A substantial proportion may be alive and
341 receiving ART from another facility, while others may have died but were not reported as such
342 [33,34]. This may be achieved through strengthening the current active patient tracking and
343 tracing mechanisms [35]. The existing ART programme's electronic patient monitoring
344 systems (ePMS) should also be scaled up and optimised to bring efficiency in patient
345 monitoring [36]. Tracing mechanisms include SMS reminders, phone calls and home visits by
346 community health workers [37].

347
348 There was a change in the risk factors for attrition in comparison to the previous evaluation.
349 Males were at risk of attrition in the prior evaluation but were not risk in the current evaluation.
350 Several studies have consistently showed males at high risk of attrition due to several reasons,
351 including employment related constraints and poor health seeking behaviour leading to late
352 presentation [13,15,38]. During the study period the country did not implement many specific
353 interventions that targeted men. Decentralisation of ART services may have also worked in

354 favour of males for better retention as they could now access services at health facilities closer
355 to where they reside. Another strategy that may have improved male ART uptake and retention
356 was male involvement in PMTCT (Option B+), promoted during massive campaigns [19].
357 There is a need for further studies to assess whether this strategy suffices, or if other strategies
358 targeting men are needed, such as flexible clinic hours to accommodate work, community-
359 based ART delivery, and tracing of those who miss appointments[39,40].

360

361 The previous evaluation did not include data on adolescents and young adults [17]. We found
362 that adolescents and young adults were more at risk of attrition when compared to adults. Our
363 findings are consistent with other studies [41–43]. Adolescents and young adults have been
364 shown to be at high risk of attrition due to several factors, which include lack of youth-friendly
365 services, rigid scheduling not taking into account schooling, and unavailability of peer
366 caregivers [44,45]. Addressing these challenges can lead to improvement in the retention of
367 adolescents and young adults on ART. Locally, community adolescent treatment supporters
368 (CATS) have been shown to improve retention among adolescents and scaling up of the
369 initiative should be prioritised [46].

370

371 We found patients with advanced disease to be at higher risk of attrition. Patients with advanced
372 HIV disease are prone to attrition mainly due to mortality and morbidity. The common causes
373 of morbidity and mortality in low resource setting include cryptococcal meningitis,
374 tuberculosis, sepsis, malignancy and wasting syndrome/chronic diarrhoea [47–49]. Advanced
375 HIV disease was also a risk factor for attrition in the previous evaluation. Very minimal
376 investment in building capacity at primary health facilities in the management of patients with
377 advanced HIV disease contributes to poorer outcomes in this subgroup. Indeed, access to
378 baseline CD4 testing, screening and management of opportunistic (tuberculosis, cryptococcal

379 meningitis) and access to prophylaxis (isoniazid preventive therapy & pre-emptive
380 fluconazole) remains a challenge in the Zimbabwe's public sector [50,51]. Recent evidence has
381 also shown that screening, prophylaxis and management of opportunistic diseases (mainly
382 tuberculosis, bacterial sepsis and cryptococcal disease) significantly reduce morbidity and
383 mortality [52,53]. However, evidence from this enhanced care package is currently being
384 poorly implemented by most ART programmes in low resource setting [54]. There is a need to
385 mobilise resources for training and capacity building of health workers, setting up the necessary
386 infrastructure and procurement of the necessary commodities required in the management of
387 patients with advanced disease. However, the process should be guided by a formal assessment
388 of the current burden of advanced disease in the country.

389

390 We also found that patients who started ART after 2013 to be at risk of attrition as compared
391 to those who started prior. We speculate that this could be explained by the fact that patients
392 were now starting ART at a higher CD4 count. In 2013, the country switched ART guidelines
393 to the 500 CD4 cells per cubic millilitres threshold from the 350 cells per cubic millilitres cut-
394 off which was used in 2012. On top of the change in the CD4 cut off point, test and treat was
395 also introduced to specific sub-populations (children under 5 years, TB/HIV co-infected,
396 HBV/HIV co-infected, the HIV-positive partner in HIV sero-discordant relationship and
397 pregnant and breastfeeding mothers (Option B+). Similar findings were reported in previous
398 studies, which showed that patients who started ART at a higher CD4 were at risk of
399 attrition[8,9]. Patients starting ART at high CD4 are less sick and have low risk perception
400 which might affect adherence to long term therapy [55]. This then calls for earnest
401 implementation of the current country operational guidelines which recommends adequate
402 psychosocial preparation and readiness assessment before ART initiation under Treat All [37].

403

404 Our study was a follow-up evaluation of the Zimbabwe ART programme. To our knowledge,
405 no studies showing national data have been followed-up by a second study of similar
406 magnitude. In a recent review, none of the studies included was a follow-up to a prior
407 evaluation [5]. Despite the highlighted strengths our study had limitations. Most of the reported
408 attrition was due to LFTU. Patients who are classified as LTFU might have been alive and still
409 on ART (self-transferred), stopped ART or may have died [32]. Our LTFU definition (180
410 without visit) differed from the one used by the program (LTFU = 90 days late), due to data
411 availability. However, considering that patients received up to 3 months ART refill, both
412 definitions would result in similar findings. Moreover, we could not report on immunologic
413 and virologic patient outcomes due to missing information in the patient manual medical
414 records. Information on viral load testing and CD4 testing was missing.

415 Conclusion

416 Zimbabwe's ART program shows good retention across different patient groups. The ART
417 retention increased since the previous 2011 evaluation. However, adolescents and young
418 adults, patients with advanced HIV disease (WHO Stage 4, impaired functional status),
419 receiving care at PHC level and starting treatment after 2013 when the country switched
420 treatment guidelines to the 500 CD4 cells per cubic millilitres threshold were at risk of attrition.

421 From the findings we recommend research into the following areas: reasons for higher attrition
422 at PHC facilities, feasibility of screening for advanced disease at primary health facilities and
423 ensuring access to referral clinical care, assessing retention within levels of care, qualitative
424 research to explore the causal link between attrition in recent years, and being less sick at the
425 start of treatment. To improve monitoring electronic patient monitoring systems should be
426 prioritised to aid patient tracking. There is also a need for differentiated care strategies for
427 adolescents and young adults to improve retention. Creation of youth-friendly services, flexible

428 scheduling of visits and expansion of peer caregivers/treatment supporters should be
429 considered.

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444

445 **Authors Contributions**

446

Author	Contribution
Richard Makurumidze	Conceptualization, Data curation, Formal analysis, Methodology, Validation, Writing – original draft preparation,
Tsitsi Mutasa-Apollo	Conceptualization, Data curation, Methodology, Project administration, Supervision, Writing – review & editing,
Tom Decroo	Conceptualization, Data curation, Validation, Formal analysis, Methodology, Writing – review & editing

Regis C. Choto	Conceptualization, Data curation, Methodology, Project administration, Supervision, Writing – review & editing
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Wim Van Damme	Conceptualization, Methodology, Writing – review & editing
James Hakim	Conceptualization, Methodology, Writing – review & editing
Tapuwa Magure	Project administration, Supervision, Resources, Funding Acquisition
Owen Mugurungi	Project administration, Supervision, Resources, Funding Acquisition
Simbarashe Rusakaniko	Conceptualization, Data curation, Methodology, Data Analysis, Supervision, Validation, Writing – review & editing

447

448 **Data Availability**

449 The study was conducted with routinely collected data of the Zimbabwe National ART
450 Programme and anonymized individual patient level data. Permission to conduct the study and
451 ethical clearance were obtained from the Ministry of Health & Child Care and the Medical
452 Research Council of Zimbabwe. Permission was also sought to disseminate the results in
453 relevant scientific forums. However, the data which was used to conduct is not available on the
454 public domain and anyone interested in using the data for scientific purpose is free to request
455 permission from the Director of the AIDS and TB Program, Dr Owen Mugurungi, Director of
456 the AIDS and TB Program, AIDS and TB Unit, Ministry of Health and Child Care,
457 Government of Zimbabwe, 2nd Floor, Mukwati Building, Harare, Zimbabwe. E-mail:
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465

466 **Competing Interests**

467 The authors declare that they have no competing interests.

468

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653

Targeted number of records to be abstracted

bioRxiv preprint doi: <https://doi.org/10.1101/750232>; this version posted August 28, 2019. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY 4.0 International license.

4000

7 records were not reviewed

Actual number records abstracted

3993

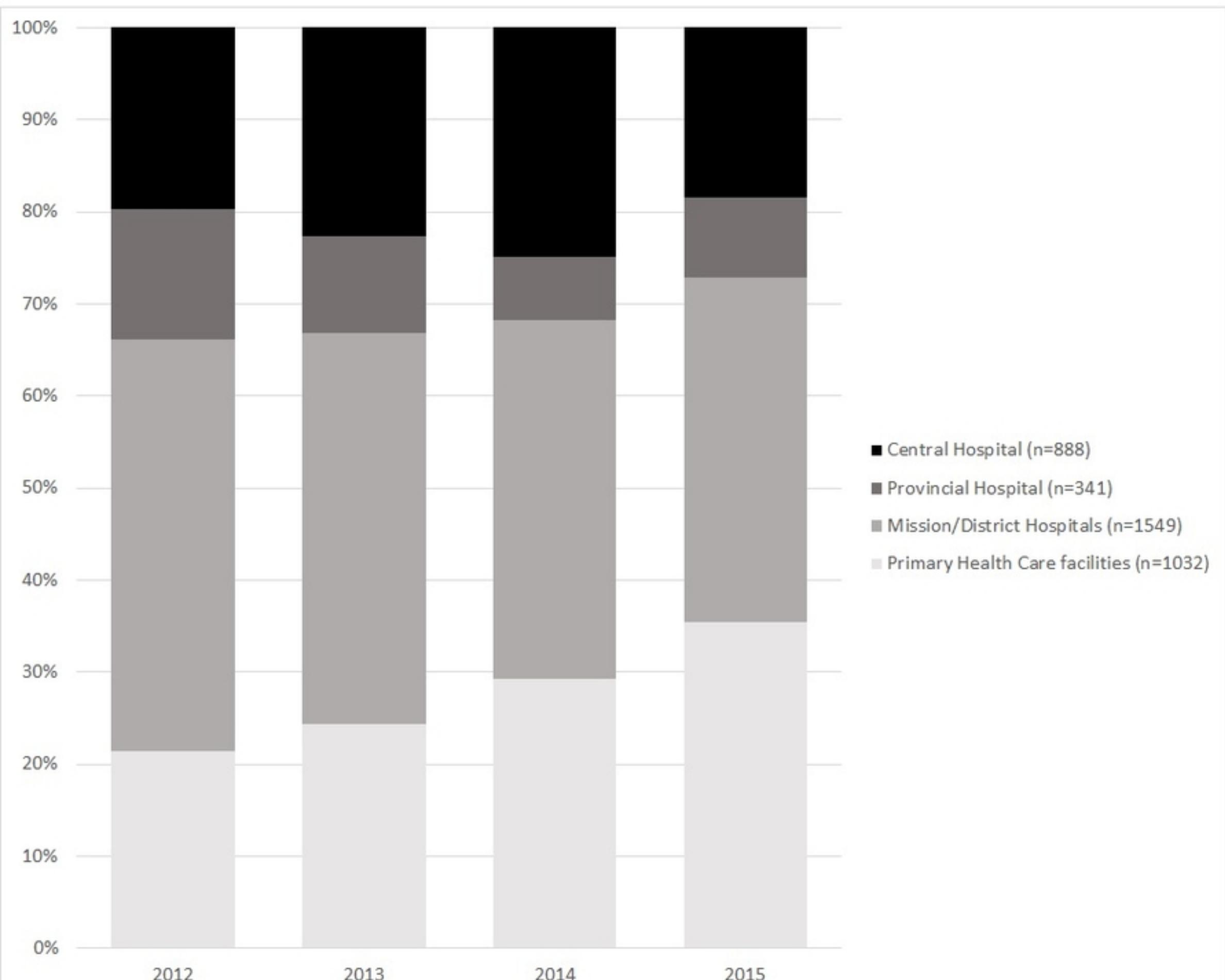
183 records dropped

- Patients enrolled before 1 October 2012
- Patients enrolled after 31 January 2015
- ART start date missing
- Last visit/outcome date missing
- Patients in care for less than 6 months

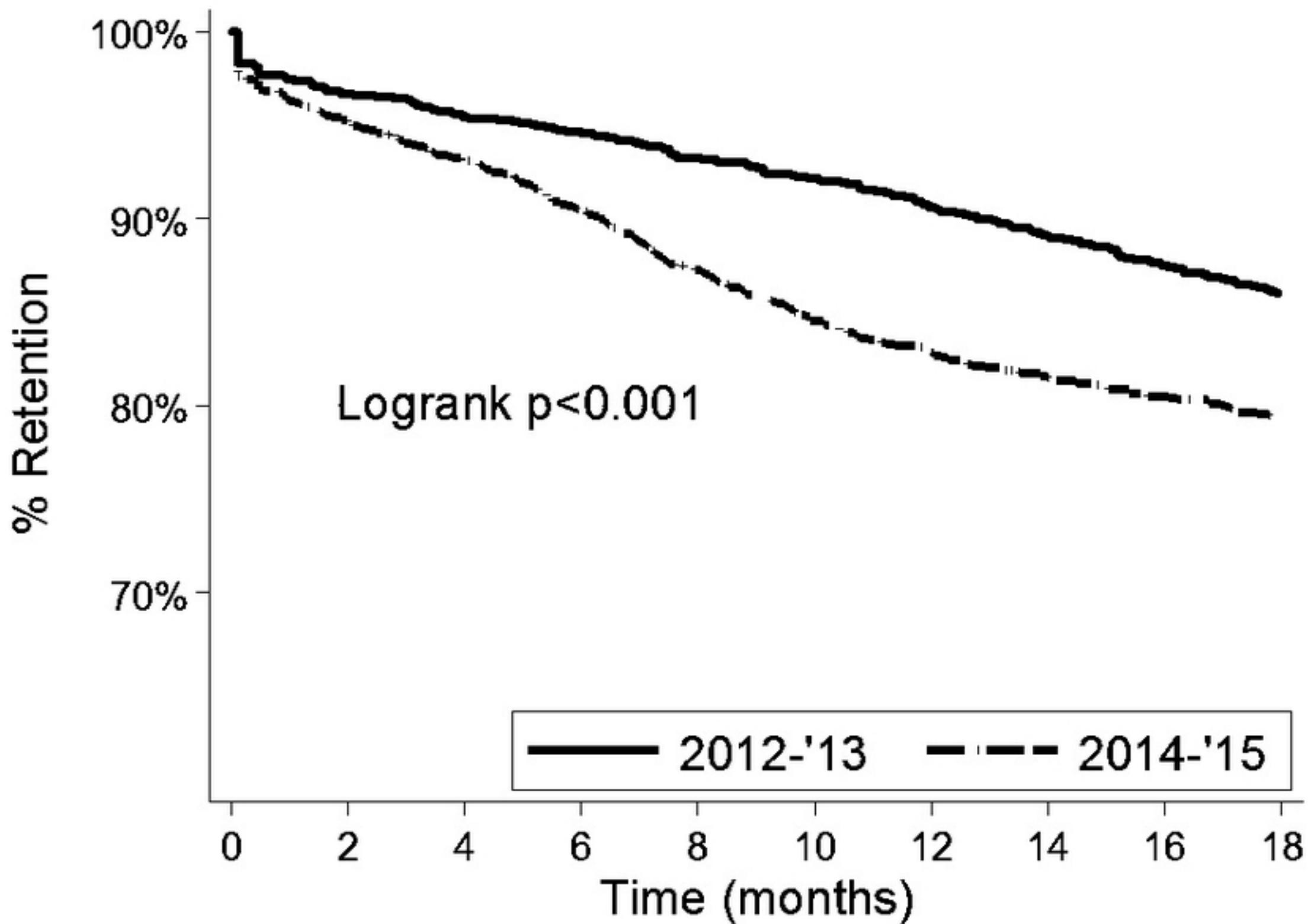
Number of records finally analysed

3810

Figure



Figure



Figure