Cervical Cancer Screening Cascade for women living with HIV: a cohort study from Zimbabwe

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Keywords: Cascade, cervical screening, HIV/AIDS, monitoring, WHO targets, Zimbabwe

Word count:

Abstract: 249/250

Main text: 2999/3000

ABSTRACT

Background. We defined a cascade of cervical screening to evaluate the number of women living with HIV (WLHIV) achieving each cascade stage at an HIV care and treatment clinic in Zimbabwe.

Methods. We included women aged ≥ 18 years enrolled at the Newlands Clinic in Harare from June 2012 to June 2017 and followed them until June 2018. The cascade consists of screening and preventative treatment arms based on initial screening results. We report percentages, the median time to reach cascade stages, and cumulative incidence at two years with 95% confidence intervals (CI).

Results. A total of 1624 women were included in the study. In the screening arm, the cumulative incidence of cervical screening was 85.4% (95% CI 83.5-87.1) at two years. In the preventative treatment arm, the cumulative incidence of treatment after a positive screening test was 79.5% (95% CI 75.1-83.2) at two years. Half of the treated women received cryotherapy (152/316, 48.1%, median time to treatment=0 days, interquartile range 0-15). The cumulative incidence of testing negative at re-screening after treatment was 36.1% (95% CI 31.2-40.7) at two years. Cervical cancer was diagnosed in 15 women; all were referred for further treatment.

Conclusions. Analyzing outcomes along the proposed Cervical Cancer Screening Cascade can identify areas for improvement. Interventions are needed to improve linkage to treatment for screen-positive women who do not qualify for same-day cryotherapy. Many women continued to screen-positive after treatment. Further studies are needed to understand the significance and potential consequences of these positive tests among WLHIV.

60 INTRODUCTION

61 Screening programs must be scaled up in low- and middle-income countries (LMIC) to reach the 2030 World
62 Health Organization (WHO) targets for eliminating cervical cancer [1–3]. Many sub-Saharan African countries
63 introduced pilot screening programs in the 1990s. Still, cervical cancer remains the most common cancer
64 among women [4]. In Zimbabwe, over 2000 cervical cancer cases are recorded each year, and this is considered
65 a significant under-estimation [5–7]. Furthermore, women with cervical cancer usually present at late stages
66 of the disease, resulting in high morbidity and mortality [8].

67 Cervical cancer incidence and mortality decrease when screening programs engage and retain women from
68 screening to treatment to follow-up along a care continuum [9, 10]. Studies of the HIV care cascade have
69 identified bottlenecks undermining the scale-up of antiretroviral therapy (ART) [11–13], which provides
70 researchers, clinicians and policymakers with essential information for context-specific reforms [14,15]. A
71 cascade approach to monitoring cervical screening programs could especially benefit women living with HIV
72 (WLHIV) who are at higher risk of human papillomavirus (HPV) infection and require repeat treatments [16–
73 19].

74 We defined and assessed a Cervical Cancer Screening Cascade for WLHIV enrolled at an ART clinic in Harare,
75 Zimbabwe and explored patient factors associated with retention through stages of the cascade.

76

77 METHODS

78 Study design

79 This retrospective cohort study used routinely collected data from an HIV care and treatment clinic in Harare,
80 Zimbabwe.

81 Study site

82 The Newlands Clinic (<https://www.newlandsclinic.org.zw>) is an HIV/AIDS referral clinic run by a Swiss
83 charitable organization ([Appendix 1](#)). The cervical screening program was established in 2011, using primarily
84 visual inspection with acetic acid and cervicography (VIAC) ([Appendix 1](#)). A Papanicolaou (PAP) test is
85 performed when the transformation zone is not visible, and biopsies are taken of ambiguous lesions or those
86 suspicious of cancer. Nurses treat small precancerous lesions with cryotherapy on the same day as screening
87 [20]. Once a week, a gynecologist performs loop electrosurgical excision procedures (LEEP) and provides a
88 second opinion on cervical images if needed. Newlands Clinic adheres to the following screening schedule:
89 first screening test within 12 months of enrollment and re-screen within 12 months if the first test is negative.
90 For a positive test, women are treated within six months and re-screened within six months of treatment.

91 Eligibility criteria

92 We included all women aged 18 years or older who had their first ART clinic visit between June 2012 and June
93 2017 (“women in care”). We allowed for a one-year follow-up, with data collection ending in June 2018. The
94 cohort was identified through the clinic’s electronic patient-care system.

95 Cascade stages

96 We focused on secondary prevention and defined a Cervical Cancer Screening Cascade, composed of
97 “screening” and “preventative treatment” arms ([Figure 1](#)). The screening arm follows women in HIV care
98 through screening and re-screening after a negative screening result. Its stages are defined as the number of
99 women: (i) in care and eligible for screening; (ii) screened for cervical cancer; (iv) with documented screen-
100 negative results at their first screening; (v) screen-negative who re-screened; (vi) with documented screen-
101 negative results at re-screening. The preventative treatment arm follows women in HIV care through screening
102 and re-screening after a positive screening result. Its stages are defined as the number of women: (i) with
103 documented screen-positive results at first screening; (ii) receiving treatment; (iii) treated who were re-
104 screened; (iv) treated with documented screen-negative results at re-screening ([Figure 1](#)). Women may be
105 diagnosed with cervical cancer throughout the cascade ([Figure 1](#), defined in [Appendix 2](#)). After cancer
106 diagnosis, women are referred for tertiary prevention and exit the Cervical Cancer Screening Cascade.

Data extraction and management

We extracted data on screening (VIAC results, PAP tests), treatment, and follow-up for all women in care (Appendix 3). Data on VIAC results, HIV status including CD4 and HIV RNA viral load, demographic characteristics were exported directly from the electronic patient-care system. We manually extracted data on sexual and gynecological history, cytology and histology results, referral and re-screening history, and cervical cancer management from electronic free-text fields into an EpiData database (v4.2.0.0 EpiData - Comprehensive Data Management and Basic Statistical Analysis System. Odense Denmark). Test results for VIAC were classified as positive or negative. Indeterminate cases and those suspicious for cancer were recorded as positive. The clinic gynecologist subsequently reviewed these women. Biopsies were obtained if required, and women with cervical cancer were referred for tertiary treatment. We classified PAP tests as negative when low-grade squamous intraepithelial lesions (LSIL) or atypical squamous cells of undetermined significance (ASC-US) were found. We considered (i) high-grade squamous intraepithelial lesion (HSIL); (ii) atypical squamous cells-HSIL (ASC-H) cannot be excluded; (iii) LSIL, cannot exclude HSIL (LSIL-H); (iv) persistent LSIL/ASC-US; or (v) atypical glandular cells (AGC) as positive PAP tests. In the analysis, positive VIAC tests or PAP tests were considered screen-positive.

Statistical analysis

We used descriptive statistics to report baseline patient characteristics. We report percentages for all stages of the cascade 1) with a fixed-denominator of all women enrolled in care, which remained constant throughout all stages (denominator-denominator) and 2) with a changing-denominator, where all women reaching a given stage are the denominator for the next stage (numerator-denominator). We used guideline-indicated time-frames in these analyses (Appendix 2).

We also calculated cumulative incidence for reaching each cascade stage. The first clinic visit was the start date of the screening arm of the cascade, and the date of a positive test at the first screening was the start of the preventative treatment arm. Observation time ended on the date a cascade arm was completed, the date a woman was determined lost to follow-up (120 days after she missed her last ART clinic appointment), the date of a woman's cervical cancer diagnosis or death, or the end of the study period, whichever came first. We used R-package "longitudinalcascade" [20] to calculate cumulative incidences, treating different arms, death, and cervical cancer as competing risks. We report cumulative incidences as percentages with 95% confidence intervals (CI) calculated on the log-survival scale. We also report the median time to reach specific cascade steps.

137 We used univariable Cox proportional hazard regressions to calculate cause-specific hazard ratios with 95%
138 CIs for factors associated with achieving cascade stages. In multivariable analyses, we included variables with
139 p-value < 0.05 in univariable analyses and known determinants of cervical neoplasia and retention in care (i.e.,
140 parity, employment, HIV clinical stage) [21–23]. Missing data were excluded from the analysis. We used STATA
141 v14.0 (College Station, TX: StataCorp LP) and R (R Foundation for Statistical Computing, Vienna, Austria) for all
142 analyses and figures.

143 Ethics

144 We obtained ethical approval from local IRBs (Medical Research Council of Zimbabwe: MRCZ/A/1336,
145 Cantonal Ethics Committee of Bern, Switzerland: PB_2016-00273).

146

147 RESULTS

148 Characteristics of included women

149 Of 1649 women referred to Newlands Clinic between June 2012 and June 2017, 1624 (98.4%) attended the
150 ART clinic and were included in the analysis ([Appendix 4](#)). Their median age was 37 years (IQR 29-44) ([Table](#)
151 [1](#)). Most women had two children (IQR 1-4), almost half did not use contraceptives (42.4%, n=684), and most
152 were single, widowed or divorced (57.6%, n=931). Most women had at least high-school education (87.3%,
153 n=1403) and were unemployed (54.2%, n=875). Many were already on ART at their first clinic visit (56.4%,
154 n=911) and were in WHO HIV/AIDS stage 1 (55.2% n=892).

155 Proportions along the cascade

156 [Figure 2](#) shows the percentage of women reaching each stage of the cascade within guideline-indicated time-
157 frames using fixed- (denominator-denominator) and changing-denominator (numerator-denominator)
158 approaches, respectively. Using the changing-denominator approach, 78.7% (n=1278/1624) of women were
159 screened within one year of enrollment at the clinic, and 70.8% (n=906/1278) had documented negative
160 screening results. Among screen-negative women, 73.5% (n= 666/906) were re-screened after 12 months, and
161 of these women, 90.7% (n=604/666) had documented screen-negative results. Among 372 women who were
162 screen-positive at the first screening, 78.0% (n=290/372) were treated within 6 months. Among treated
163 women, 79.7% (n=231/290) were followed up within 6 months; and 58.9% (n=136/231) had documented
164 screen-negative results. Using a fixed-denominator, the percentage decrease from one stage to the next
165 (Figure 2).

Cumulative incidences along the cascade

Total observation time was 1483 person-years (median 389 days, IQR 0-1959 days). During the study period, 1385 women were screened at least once (Appendix 5), and the median time to screening from enrollment was 63 days (IQR 28-146). [Figure 3](#) shows the cumulative incidence of reaching each stage of the cascade arms over two years. The cumulative incidence of receiving cervical screening within two years after clinic enrollment was 85.4% (95% CI 83.5-87.1). Of the screened women, 989 (71.4%) had a documented negative screening result at their first screening visit. The median time to documented negative test was 63 days (IQR 28-154), and the cumulative incidence of documented negative test within two years was 60.6% (95% CI 58.1-62.9). Among women who screened negative at the first screening, 791 (80.0%) received re-screening over the full study period. The median time from the first screening date to re-screening was 374 days (IQR 361-424), and the cumulative incidence of re-screening at two years was 44.9% (95% CI 42.3-47.3). At the time of re-screening, 713 (90.1%) remained screen-negative, and the cumulative incidence of negative re-screening was 40.6% (95% CI 38.1-43.0) at two years.

At their first screening, 396 women had documented positive screening results, and the median time to documented positive test was 64.5 days (IQR 28-133). Among women who screened positive, 316 (79.8%) were treated over the study period; from the first screen-positive test, the median time to treatment was 13 days (IQR 0-31) and the cumulative incidence of being treated within two years of a positive test was 79.5% (95% CI 75.1-83.2). Fourteen women had their treatment deferred due to pregnancy, sexually transmitted co-infection (STI) or prioritized HIV treatment and therefore exited the cascade ([Appendix 6](#)). Overall, 277 (87.7%) women were followed up after treatment, time to re-screening was 188 days (IQR 181-223), and cumulative incidence of re-screening within two years was 61.7% (95% CI 56.6-66.3). Among 277 women followed up after treatment of precancerous cervical lesions, 169 (61.0%) had documented screen-negative results and the cumulative incidence of testing negative at re-screening at two years was 36.1% (95% CI 31.2-40.7). Notably, half of the women receiving treatment received cryotherapy (n=152/316, 48.1%), usually on the same day as screening (median time to cryotherapy: 0 days, IQR 0-15). The median time to treatment for the remaining LEEP treatments was 26.5 days (IQR 9-58). Similarly, among women who tested negative at the post-treatment re-screening, 56.2% (n=95/169) had been treated with cryotherapy and 43.8% (n=74/169) with LEEP ([Appendix 7](#)). During the study period, 117 women died of any cause; median time to death was 133 days after enrollment (IQR 52-421).

Cancer diagnoses

196 Fifteen women were diagnosed with cervical cancer and were referred for treatment during the study period;
197 the median time to cancer diagnosis was 24 days (IQR 0-239). Three women received subsequent radical
198 hysterectomy, five received combination chemo-radiotherapy, one radiotherapy, and one chemotherapy.
199 Treatment of the remaining five women was unknown. By the end of the study period, seven of these women
200 died, seven were alive, and one was lost to follow-up.

201 **Factors associated with retention**

202 We assessed patient factors associated with retention in the cascade defined as attending re-screening in
203 either arm ([Table 3](#)). Women were more likely to be retained between 2015-2018, compared to 2012-2015
204 (aHR 1.26, 95% CI 1.10-1.43). Women with high HIV RNA viral loads (>1000 vs <50 copies/mm³, aHR 1.33, 95%
205 CI 1.16-1.53) and more children (parity 1-3 vs 0, aHR 1.46, 95% CI 1.15-1.86) were more likely to be retained
206 in the cascade. There was no evidence for an association of the patient factors we assessed and having a
207 negative re-screening test result after treatment ([Appendix 8](#)).

208 209 **DISCUSSION**

210 We defined a cascade to assess cervical screening in WLHIV and applied it to women enrolled in a large ART
211 program in Harare, Zimbabwe, between 2012 and 2018. The cumulative incidence of screening at two years
212 after the first clinic visit was 85%. Similarly, it was 80% for treatment at two years after screening positive.
213 Finally, the cumulative incidence of a negative test was 36% at two years after initial screen-positivity.

214 An important strength is that this is a denominator-denominator linked longitudinal study, in a single, well
215 defined population [14]. We evaluate the entire Cervical Cancer Screening Cascade using individual patient-
216 level data from routine care, extending from previous research [24–29]. The analysis of cumulative incidence
217 has the advantage of appropriately taking into account censoring and competing events. In our study, few
218 women died, developed cervical cancer, or were lost to follow-up; therefore, the cumulative incidences are
219 similar to the analysis of simple percentages. Our study also illustrates the cascade using simple percentages
220 and these could be calculated using aggregate data in sites with limited capacity to collect longitudinal patient-
221 level data on cervical cancer screening. When a fixed-denominator is used, there is internal consistency, and
222 the continuum of care across the cascade relates to the single most important denominator, women in care
223 [14]. In contrast, when a changing-denominator is used [1,9,13], problems with retention (retention gaps) at
224 different stages of the cascade are highlighted [25,26].

225 Our study has several limitations. While Newlands Clinic is an excellent setting to test the cascade concept,
226 the results may not apply to other clinics. The retention gaps between eligibility and reaching cascade stages
227 ([Figure 2](#), grey area) were not fully explained based on the data collected in our study. Data explaining reasons
228 for reduced retention across the Cervical Cancer Screening Cascade stages may improve the longitudinal
229 approach. We focused on a cascade for secondary prevention; however, increasing the cascade's breadth to
230 include vaccination and care for women diagnosed with cervical cancer would further inform cervical cancer
231 control strategies.

232 Integrating cervical cancer screening and management into HIV care can improve access for high-risk WLHIV
233 and may contribute to more risk-stratified approaches [30]. Our study overcame some limitations of previous
234 studies describing the cervical screening continuum [24–29]. Only one study illustrated a full cascade
235 graphically [24]. In contrast, previous studies focused on specific stages of the cascades (e.g. initial screening
236 results [25,29], referrals [28,31], treatment [25,26]). Previous studies did not analyze the time to reaching a
237 stage even when studies spanned several years [24,27,29]. Our longitudinal approach allowed appropriate
238 time-to-event analyses and avoided truncations to standardize the period of reaching each stage. This
239 approach offers a deeper understanding of women's movement through the cascade and may document
240 changes in the population and health system over time. Similar retention gaps have been identified in other
241 studies between screening and treatment [24,26,28,29], which is more pronounced when an interim triage
242 test (e.g. colposcopy) is also required [25,27,28]. No other studies included re-screening measures.

243 The WHO posits two national screening targets for the secondary prevention of cervical cancer: 70% of WLHIV
244 should be screened with a high-performance test from 25 years, and 90% of women who screen-positive
245 should be treated [1]. More than 70% of women aged 18 years and above, seen at Newlands Clinic, were
246 screened using the screening tests available over the study period; VIAC or PAP-smear. However, only 80% of
247 those who screened positive were treated. We do not know the intended treatments for those missed. Still,
248 because clinic guidelines adhere to a see-and-treat principle, we presume missed treatments were more likely
249 LEEP because cryotherapy would have been applied on the same day as screening. Interventions to improve
250 adherence to treatment for women who do not qualify for same-day cryotherapy may help the program reach
251 the WHO target. Still, more research is needed to understand this treatment gap and to change policies
252 accordingly.

253 Preventing cervical cancer depends on effective treatment of precancerous lesions. Few women had a
254 negative test result at post-treatment re-screening (36% at two years). This is in line with recent studies
255 reporting high treatment failure among WLHIV [32,33,34]. Most women in our study were seen after

256 treatment by seven months, so it would be unlikely, though not impossible, that new disease would develop
257 in such a short time frame. The risk of residual or recurrent cervical disease is higher in WLHIV if they are
258 treated with cryotherapy instead of LEEP [32,34], and also when the excision is incomplete [35,36], but post-
259 treatment follow-up recommendations do not vary by treatment modality. ART status and immunodeficiency
260 may also be associated with differences in CIN treatment outcomes [30]. The relatively low screening test
261 accuracy of VIAC may account for over-treatment and persistent false-positive tests at re-screening. In the
262 absence of STI testing and biopsies to confirm the need for treatment, it remains difficult to quantify the
263 potential misclassification of disease. Additionally, post-treatment screening test must be delayed until an
264 HPV infection has been suppressed and tissues repair themselves, but not delayed so long for a new HPV
265 infection to develop new cervical neoplasia. A sentinel study of post-treatment screening test accuracy among
266 WLHIV in Kenya found no single test was both highly sensitive and specific: VIA sensitivity was 27% and
267 specificity 82%; HPV sensitivity was 85% and specificity 54% [32]. When the prevalence of high-risk subtypes
268 of HPV (HR-HPV) is high, implications of a positive HPV test result post-treatment are questionable, and
269 healthcare providers must weigh the benefits of repeated treatments against the risks to women of child-
270 bearing age. As the WHO has noted, the dynamics of HR-HPV infection in WLHIV are poorly understood [37].
271 We suggest future research should: (i) test the cascade approach for cervical screening more widely and
272 comparatively across sites; (ii) consider additional methods for understanding gaps in cascade stages, including
273 qualitative studies to understand poor retention; (iii) investigate HR-HPV dynamics in WLHIV and understand
274 the significance of positive tests after treatment.

275 In conclusion, analyzing outcomes along the proposed cervical screening cascade can identify areas for
276 improvement within cervical cancer screening programs. In the setting studied in Zimbabwe, interventions are
277 needed to improve linkage to treatment for screen-positive women who do not qualify for same-day
278 cryotherapy. Furthermore, in our analysis, many women continued to screen-positive after treatment. Further
279 studies are needed to understand the significance and potential consequences of these positive tests among
280 WLHIV.

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378 **Conflict of interest:**

379 The authors have no conflicts to declare.

380 **Funding**

381 Research reported in this publication was supported by the U.S. National Institutes of Health’s National
382 Institute of Allergy and Infectious Diseases, the Eunice Kennedy Shriver National Institute of Child Health and
383 Human Development, the National Cancer Institute, the National Institute of Mental Health, the National
384 Institute on Drug Abuse, the National Heart, Lung, and Blood Institute, the National Institute on Alcohol Abuse
385 and Alcoholism, the National Institute of Diabetes and Digestive and Kidney Diseases and the Fogarty
386 International Center under Award Number U01AI069924. The content is solely the responsibility of the
387 authors and does not necessarily represent the official views of the National Institutes of Health. It is also
388 supported the Swiss Agency for Development and Cooperation by the grant Advancing Cervical Cancer
389 Screening in HIV-positive women (ACCHIVE) —The Cervical Cancer Prevention and Care Cascade (award
390 number: IZP8Z0_180245, PI JB). ME was supported by special project funding (award number: 189498) from
391 the Swiss National Science Foundation.

392 **Author contributions**

393 ME, JB, ER, KT, MP conceptualized the study and contributed to grant applications. TM and MP established
394 the screening program at Newlands Clinic and oversaw all clinical work and data-collection. KT, ER AM, TS, MP,
395 and CC developed the data collection tool or collected and cleaned data. KT and LB conducted the statistical
396 analysis. All authors contributed to the interpretation of data and provided critical inputs in the draft
397 manuscript. All authors have read and approved the final manuscript.

Tables and figures

Figure 1. Conceptual model for a Cervical Cancer Screening Cascade nested in the three pillars of cervical cancer prevention: primary, secondary and tertiary

The conceptual model considers the three pillars of cervical cancer prevention: primary, secondary and tertiary. A cascade for secondary cervical cancer prevention is detailed and is the focus of this study. The screening arm is represented by the first line and box colors white to dark blue. The preventative treatment arm is represented by the second line and box colors orange to red. The definitions for stages of the cascade can be found in Appendix 2. HPV: human papilloma virus

Table 1. Patient characteristics at baseline

Characteristic	n (%) ^a
Total	1624 (100)
Age at entry into ART clinic: median (IQR), y	37 (29-44)
Missing	0 (0.0)
Sexually active at entry into ART clinic	996 (61.3)
Not sexually active at entry into ART clinic	215 (13.2)
Missing	413 (25.4)
Pregnant at entry into ART clinic	86 (5.3)
Not pregnant at entry into ART clinic	1309 (81.1)
Missing	229 (14.2)
Gravidity at entry into ART clinic: median (IQR)	3 (2-5)
Missing	0 (0.0)
Parity at entry into ART clinic: median (IQR)	2 (1-4)
Missing	0 (0.0)
Contraception at entry into ART clinic	639 (39.6)
Not using contraception at entry into ART	684 (42.4)
Missing	301 (18.6)
Marital status at entry into ART clinic	
Married	686 (42.5)
Partnership	5 (0.3)
Divorced	102 (6.3)
Widowed	328 (20.3)
Single	501 (31.0)
Missing	2 (0.1)
Education obtained at entry into ART clinic	1554 (96.2)
No education obtained at entry into ART clinic	70 (4.3)
Missing	0 (0.0)
Employment at entry into ART clinic	558 (34.6)
Student	79 (4.9)
Unemployed	875 (54.2)
Missing	112 (6.9)
WHO HIV/AIDS Stage at entry into ART clinic	
1	892 (55.2)
2	260 (16.1)
3	237 (14.7)
4	148 (9.2)
Missing	87 (5.4)
On ART at entry into ART clinic	911 (56.4)
Not on ART at entry into ART clinic	713 (44.1)
Missing	0 (0.0)
Nadir CD4 cell count: median (IQR), cells/mm³	258 (120-409)
Missing	0 (0.0)
HIV RNA viral load at entry into ART clinic: median (IQR), copies/mm³	899 (28-47,969)
Missing	58 (3.6)

IQR: inter-quartile range; AIDS: acquired immunodeficiency syndrome; ART: Antiretroviral Therapy; CD4 cell: Cluster of differentiation four cells; cells/mm³; copies/mm³: copies in a cubic millimetre; HIV: human immunodeficiency virus; n: number of women; RNA: Ribonucleic acid; WHO: World Health Organization; y: years; %: percentage; ^a: Data represent n(%) of participants unless otherwise specified.

Figure 2. Number and percentage of women for each stage of the Cervical Cancer Screening Cascade: screening and preventative treatment arms

Panel A: screening arm; left: percentages using a fixed denominator (denominator-denominator approach), referring to the denominator “women in care”; right: using a changing denominator (numerator-denominator approach), referring to all women reaching the previous stage; panel B: preventative treatment arm; left: percentages using a fixed denominator (denominator-denominator approach), referring to the denominator “screen-positive at first screening”; right: using a changing denominator (numerator-denominator approach), referring to all women reaching the previous stage. The guideline indicated timeframes are described in the Methods and Appendix 2. Grey areas represent the percentage of eligible women who did not achieve a respective cascade stage (retention gaps).

Figure 3. Analysis of cumulative incidence – percentage of women transitioning through the Cervical Cancer Screening Cascade by year

The two-year cumulative incidence of women transitioning to each stage of the Cervical Cancer Screening Cascade - Panel A: Cervical Cancer Screening Cascade, time zero: date of first ART clinic visit; Panel B: screening arm, time zero: date of first ART clinic visit; Panel C: preventative treatment arm, time zero: date of initial screen-positivity.

Table 3. Crude and adjusted hazard ratios for factors associated with retention in the Cervical Cancer Screening Cascade

	Univariable analyses n = 1251			Multivariable analysis n = 1251		
	HR	95% CI	P value	HR	95% CI	P value
Age, years						
<25	2.02	1.61-2.54	<0.001	1.40	1.07-1.82	0.025
25-44	1	-		1	-	
>45	2.19	1.71-2.80		1.50	1.12-2.03	
Relationship						
Single	0.78	0.67-0.90	0.002	0.83	0.71-0.98	0.076
Relationship	1	-		1	-	
Separated	0.98	0.85-1.14		0.92	0.78-1.08	
Employment						
Unemployed	1	-	<0.001	1	-	0.388
Employed	0.98	0.86-1.12		0.93	0.81-1.06	
Student	0.45	0.29-0.70		0.81	0.51-1.30	
Parity						
0	1	-	<0.001	1	-	0.008
1 to 3	1.77	1.44-2.19		1.46	1.15-1.86	
>3	1.37	1.08-1.73		1.41	1.07-1.85	
HIV RNA viral load at VIA screening, copies/mm³						
<50	1	-	<0.001	1	-	<0.001
50-1000	1.21	0.99-1.47		1.19	0.96-1.47	
>1000	1.36	1.19-1.55		1.33	1.16-1.53	
Calendar period enrolled						
Early years: 2012-2014	1	-	<0.001	1	-	<0.001
Later years: 2015-2017	1.31	1.16-1.49		1.26	1.10-1.43	
Nadir CD4 cell count, cells/mm³						
<200	1	-	0.977			
200-349	1.02	0.86-1.29				
350-499	1.40	1.86-1.26				
>500	1.02	0.84-1.24				
HIV RNA viral load at ART enrollment, copies/mm³						
<50	1	-	0.150			
50-1000	0.79	0.62-1.01				
>1000	0.96	0.84-1.10				

Retention in the Cervical Cancer Screening Cascade is defined as all women achieving rescreening in either arm (screening or preventative treatment) of the Secondary Cervical Cancer Prevention Cascade. HR: hazards ratio; n: number of women; CI: confidence interval; HIV: human immunodeficiency virus; RNA: Ribonucleic acid; VIA: visual inspection with acetic acid; n: number of women.

Appendices

Appendix 1. Study site details

Since 2004, Newland's Clinic has provided comprehensive healthcare services for people living with HIV. The clinic has had protocols in place to track patient response to treatment using HIV RNA viral loads supported by its own independent laboratory since 2013. The clinic also provides a wide range of additional services aiming to improve the wellbeing of their patients as well as their families. Patient nutrition is monitored, and food supplementation is provided for the family if food security cannot be guaranteed. Patients are regularly monitored for non-communicable diseases. Specialized adolescent and perinatal care with psychological supports are also available. The Clinic is based on a nurse-led model of care, with doctors supporting nurses with clinical decisions. Weekly case-based teaching for all staff, and Advanced HIV management courses for external health-care workers are offered and supported by the Ministry of Health and Child Care in Zimbabwe.

The cervical cancer screening services have been in place since January 2012. All women who are sexually active are referred to have cervical cancer screening, however this is not recorded systematically in the electronic data-base. Screening is predominantly by visual inspection with acetic acid and cervicography (VIAC). This procedure requires a vaginal speculum examination and the application of 3-5% acetic acid to the cervix. The appearance of white plaques on the surface of the cervix may indicate the presence of precancerous or cancerous disease. The cervix is examined by naked eye and images are obtained using a Cannon camera (Powershot SX40HS, 12MP CMOS sensor). Cervical images are stored in the patient notes in the clinic database, can subsequently be reviewed by a local gynecologist. If a woman is suspected of having cervical cancer, she is referred for further treatment to a tertiary center. For woman who do not have a visible transformation zone and are therefore not suitable for VIAC, a Papanicolaou (PAP) test is done. Ambiguous cervical lesions and those suspicious for cervical cancer may be biopsied. Pre-cancerous lesions of the cervix can be treated on the same day as screening by nurses who are trained in cryotherapy, if women have amenable lesions. A local gynecologist comes to the clinic weekly to provide Loop electrosurgical excision procedure (LEEP) treatment and a second opinion on cervigrams. Women with signs or symptoms of sexually transmitted infections (STIs) are offered treatment which may delay treatment of concurrent cervical lesions.

Appendix 2. Definitions for conceptual model: Secondary cervical cancer prevention cascade: screening and preventative treatment

CERVICAL CANCER SCREENING CASCADE: screening and preventative treatment			TERTIARY PREVENTION
Screening arm	Definitions		
	Cumulative incidence	Overall percentages*	
Identify target population	Number of women in care aged 18 years or older	Number of women in care aged 18 years or older	Number of women already known to have cervical cancer at enrolment
Screen target population	Number of women screened for cervical cancer	Number of women screened for cervical cancer within 12 months of enrolment	Number of women with symptoms of cervical cancer prior to scheduled screening and found to have cervical cancer
Documented negative screening results	Number of women who received screen-negative results at screening	Number of women who receive negative screening results within 12 months of enrolment	Number of women who receive screening results "suspicious for cancer" following VIA
Retain in screening	Number of screen-negative women who were rescreened	Number of screen-negative women who were rescreened within 12 months of first screening	Number of women found to have cervical cancer following histological review of treated lesions or following biopsy**
Reduce cervical cancer risk	Number of screen-negative women who received screen-negative results at rescreening	Number of screen-negative women who received screen-negative results at rescreening and were rescreened within 12 months of first screening	Symptoms of cervical cancer prior to scheduled screening and found to have interval cervical cancer

CERVICAL CANCER SCREENING CASCADE: screening and preventative treatment			TERTIARY PREVENTION
Preventative treatment arm	Definitions		
	Cumulative incidence	Overall percentages*	
Documented positive screening results	Number of women who received a positive screening result at their first screening	Number of women who received a positive screening result at their first screening within 12 months of enrolment	Number of women who receive screening results "suspicious for cancer" following VIA
Linked to treatment	Number of screen-positive women who received treatment	Number of screen-positive women who received treatment within 6 months of screening result	Number of women found to have cervical cancer following histological review of treated lesions or following biopsy**
Retain in screening	Number of treated women who were rescreened	Number of treated women who were rescreened within 6 months of treatment	Symptoms of cervical cancer prior to scheduled screening and found to have interval cervical cancer
Reduce cervical cancer risk	Number of treated women who received screen-negative results at rescreening	Number of treated women who received screen-negative results at rescreening, and were rescreened within 6 months of treatment	Number of women who receive rescreening and receive screening results "suspicious for cancer" following VIA

Appendix 3. Extraction form

The following extraction form was created *a-priori*. Below we indicate data collected for each stage of the cascade.

Please note that since this extraction form was developed, names of cascade stages have changed.

Abbreviation list

ART	antiretroviral therapy	ICC	invasive cervical cancer
ASCUS	atypical squamous cells of undetermined significance	ID	Identification
CD4	cluster of differentiation 4	IUCD	intrauterine contraceptive device
CIN	cervical intraepithelial neoplasia	LEEP	Loop Electrosurgical Excision Procedure
COCP	combined oral contraceptive pill	LLETZ	Large Loop Excision of the Transformation Zone
EUA	Examination under Anesthetic	STI	sexually transmitted infections
FU	Follow-up	VIA	Visual Inspection with Acetic Acid
HIV	human immunodeficiency virus	WHO	World Health Organization
HPV	human papillomavirus		

Baseline site data					
Question number	Variable name	Description	Format	Code	Notes
6	country	In which country is your ART program located?	Categorical	1 = Zimbabwe 2 = Zambia 3 = Malawi 4 = South Africa 5 = Mozambique 88 = other	
7	country_c	If response to country = 88, please insert country name	String		
8	site_type	Site Type (for example, HIV clinic, Maternal and Child health	String		

Baseline site data					
		clinic, Maternal and family health clinic, Sexual health clinic, antenatal clinic, clinical research site, primary care general clinic, other)			
9	affiliations	If research site, please list research networks your site is involved in and university affiliations	String		
10	site_loc	Site Location	Categorical	1 = urban 2 = rural 3 = peri-urban	
11	art_start	Date of onset of ART program	Date	YYYY-MM-DD (99 for any or all missing components)	
12	viral_loads_start	When did this clinic start measuring viral loads for monitoring HIV treatment	Date	YYYY-MM-DD (99 for any or all missing components)	
13	cx_screen_start	Date of onset of cervical screening program	Date	YYYY-MM-DD (99 for any or all missing components)	
14	data_entry_start	Years included in following survey	Date	Start date: YYYY-MM-DD (99 for any or all missing components)	
15	data_entry_end			End date: YYYY-MM-DD (99 for any or all missing components)	
16	site_level_screenby	Cervical cancer screening is done by: (more than one answer may be appropriate)	Categorical	1 = nurse 2 = lay health worker 3 = doctor other than gynecologist 4 = gynecologist 77 = don't know 88 = other	
17	site_level_screenby_c	If response to site_level_screenby = other, please describe	String		
18	ref_for_cx_screen	Women are referred to your clinic for cervical cancer screening	Categorical	0 = no 1 = yes 77 = don't know	
19	avial_via	VIA screening is available at this clinic	Categorical	0 = no 1 = yes 77 = don't know	

Baseline site data					
20	avial_via_d	Start date: VIA has been available since	Date	YYYY-MM-DD (99 for any or all missing components)	
21	avail_smear	PAP smear test can be done at this clinic	Categorical	0 = no 1 = yes 77 = don't know	
22	avail_smear_d	Start date: Smear test have been available since	Date	YYYY-MM-DD (99 for any or all missing components)	
23	avail_hpv	HPV testing can be done at this clinic	Categorical	0 = no 1 = yes 77 = don't know	
24	avail_hpv_d	Start date: HPV testing has been available since	Date	YYYY-MM-DD (99 for any or all missing components)	
25	cervicitis_tx_prot	Diagnosis and treatment of cervicitis is based on clinical signs and symptoms	Categorical	0 = no 1 = yes, mostly 2 = yes, always 77 = don't know	
26	avail_swabs	Diagnosis and treatment of cervicitis is based on cultures obtained from swabs	Categorical	0 = no 1 = yes 77 = don't know	
27	avail_swabs_d	Swabs to confirm cervicitis have been available since	Date	YYYY-MM (99 for any or all missing components)	
28	targetgroup	Women are eligible based on age, sexual activity or both of these features	Categorical	1 = age 2 = sexual activity 3 = both above	If age is selected, go to site_age_target1 If not go to screen_interval_n
29	site_age_target1	Age range of women eligible for screening at your site	Categorical	Youngest Continuous variable	
30	site_age_target2			Oldest Continuous variable	
31	identify	Eligible women can be identified by:	Categorical	1 = HIV clinic database 2 = social security register 3 = health insurance register	

Baseline site data					
				4 =health service register 88 = other	
32	invite	Are women invited to participate in cervical cancer screening opportunistically, or by another more regular/systematic method	Categorical	1 = opportunistic 77 = don't know 88 = other	
33	invite_c	If a method other than Opportunistic invitation is used, please describe it	String		
34	invite_method	Methods used to invite women (select all applicable)	Categorical	1 = letter 2 = phone call 3 = verbally at clinic 4= following campaign drives 77 = Don't know 88= other	
35	data_stored	Screening data is stored (select all applicable)	Categorical	1 = electronic, 2 = paper-based, 77 = don't know, 88 = other	
36	data_stored_c	If screening is stored by another means please describe	String		
37	data_stored_invite	Do you capture data on whether a woman is invited for cervical screening or not? (for example, is this recorded as text or on the database as a specific variable for each patient)	Categorical	0 = no 1 = yes 77 = don't know	
38	screen_interval_n	Recommended screening interval in clinic when previous smear normal (Please indicate in YEARS or MONTHS)	String		
39	screen_interval_tx	Recommended screening interval in clinic when previous treatment for precancerous lesions (Please indicate in YEARS or MONTHS)	String		

Baseline site data					
40	price_screen	What is the price that each women pays out of their own pocket for an initial screening visit at your clinic? (please include the currency)	String (currency)		
41	cryo_tx	Can women receive cryotherapy treatment at your clinic	Categorical	0 = no 1 = yes 77 = don't know	
42	leep_tx	Can women receive LEEP treatment at your clinic	Categorical	0 = no 1 = yes 77 = don't know	
43	price_cin_tx	What is the price that each woman pays out of pocket for cryotherapy treatment? (please include the currency)	String (currency)		
44	cancer_tx	Which cancer treatments are offered by your clinic? (select all applicable)	Categorical	0 = none 1 = Surgery 2 = Chemotherapy 3 = Radiotherapy 4 = hospital-based palliation 5 = home-based palliation 77 = don't know	
45	ref_cancer_tx	Which cancer treatments are available to patients by referral? (select all applicable)	Categorical	0 = none 1 = Surgery 2 = Chemotherapy 3 = Radiotherapy 4 = hospital-based palliation 5 = home-based palliation 77 = don't know	
46	price_cancer_tx	Please explain how cancer treatment is funded describing both Government contributions and the price women must pay out of pocket?	String		

Patient level screening data for women in ART programs

Please include data on **all women, 18+ years of age, entering HIV care** between the start and end dates of your survey.

Cascade step 1: Identification Baseline patient data

Nr	Variable name	Description	Format	Code	Notes
100	pid	Patient ID: Code to identify patient (Cohort Patient ID)	Numeric	Continuous variable 99 = not recorded	This data pertains to ALL WOMEN, 18 YEARS OF AGE AND OLDER, ENTERING HIV CARE over the FULL period of the study
101	center	Clinic code: Code for Clinic/Centre/Hospital where patient is seen. Needs to be unique within each region.	String		
102	nat_n	Country of Origin/nationality	Categorical	1 = Zimbabwean 2 = Zambian 3 = Malawian 4 = South African 5 = Mozambican 88 = other 99 = not recorded	
103	nat_c		String	If response to nat_n = 88, state nationality	
104	bd	Birth date of woman	Date	YYYY-MM-DD (99 for any or all missing components)	
105	ed	Education level at time of enrollment into ART program	Categorical	0 = none 1 = primary 2 = high school 3 = university/ college 99 = not recorded	
106	marital	Marital status at time of enrollment into ART	Categorical	1 = single 2 = married 3 = widowed 4 = divorced 5 = partnership 99 = not recorded	
107	s_active	Woman is sexually active at enrollment into ART program	Categorical	0 = no 1 = yes 99 = not recorded	

Patient level screening data for women in ART programs

Please include data on **all women, 18+ years of age, entering HIV care** between the start and end dates of your survey.

Cascade step 1: Identification Baseline patient data

108	pregnant	Woman is sexually active at enrollment into ART program	Categorical	0 = no 1 = yes 99 = not recorded	
109	employ	Employment status at time of enrollment into ART (tick all relevant)	Categorical	0 = unemployed 1 = employed 2 = self-employed 3 = student 99 = not recorded	
110	smoke	Cigarette smoking status at time of enrollment into ART	Categorical	0 = never smoked 1 = current smoker 2 = ever smoked 99 = not recorded	
111	gravid	Gravidity (the number of times that a woman has been pregnant) at time of enrollment into ART	Numeric	Continuous variable 99 = not recorded	
112	parity	Parity (the number of times that she has given birth to a fetus with a gestational age of 24 weeks or more, regardless of whether the child was born alive or was stillborn) at time of enrollment into ART	Numeric	Continuous variable 99 = not recorded	
113	contraception	Contraception at time of enrollment into ART	Categorical	0 = none 1 = combined oral contraceptive pill (COCP) 2 = intrauterine contraceptive device (IUCD) 3 = Depo-Provera (progestin injection received 3 monthly) 4 = implant (small subdermal progestogen rods – usually effective for 3 -5 years) 5 = condoms 88 = other 99 = not recorded	

Patient level screening data for women in ART programs

Please include data on **all women, 18+ years of age, entering HIV care** between the start and end dates of your survey.

Cascade step 1: Identification Baseline patient data

114	contraception_c	If response to contraception = 88, describe	String		
115	nadir_cd4	Nadir cd4 from clinic records	Numeric (cells/ μ l)	Continuous variable 99 = not recorded	
116	nadir_cd4_d	Date Nadir cd4 obtained	Date	YYYY-MM-DD (99 for any or all missing components)	
117	vl_art	Viral load at time of enrollment into ART program, (closest to enrollment)	Numeric (copies/ml)	Continuous variable 99 = not recorded	
118	vl_art_d	Date viral load at enrolment into ART obtained	Date	YYYY-MM-DD (99 for any or all missing components)	
119	vl_via	Viral load at time of first VIA	Numeric	Continuous variable 99 = not recorded	
120	vl_via_d	Date viral load at time of first VIA obtained	Date	YYYY-MM-DD (99 for any or all missing components)	
121	hist_sti	Previous STI reported verbally	Categorical	0 = no 1 = yes 99 = not recorded	
122	hist_sti_d	Date of hist_sti	Date	YYYY-MM-DD (99 for any or all missing components)	
123	swabs1	Swabs done at time of first VIA	Categorical	0 = no 1 = yes 99 = not recorded	
124	swabs1_n	STIs found on clinically obtained swabs at time of first VIA (select all relevant)	Categorical	0 = no growth 1 = trichomonas 2 = chlamydia 3 = candida 4 = Gonorrhea 5 = HSV 6 = indeterminate results 88 = other 99 = not recorded	

Patient level screening data for women in ART programs

Please include data on **all women, 18+ years of age, entering HIV care** between the start and end dates of your survey.

Cascade step 1: Identification Baseline patient data

125	swabs1_d	Date swabs obtained	Date	YYYY-MM-DD (99 for any or all missing components)	
126	swabs1_c	If response to Swabs1_n = 88, describe	String		
127	swabs2	Swabs done subsequently to swabs1_d	Categorical	0 = no 1 = yes 99 = not recorded	
128	swabs2_n	STIs found on clinically obtained swabs at time of second VIA (select all relevant)	Categorical	0 = no growth 1 = trichomonas 2 = chlamydia 3 = candida 4 = Gonorrhea 5 = HSV 6 = indeterminate results 8 = normal 88 = other 99 = not recorded	
129	swabs2-d	Date swabs obtained	Date	YYYY-MM-DD (99 for any or all missing components)	
130	swabs2_c	If response to Swabs2_n = 88, describe	String		
131	swabs3	Swabs done subsequently to swabs2_d	Categorical	0 = no 1 = yes 99 = not recorded	
132	swabs3_n	STIs found on clinically obtained swabs at time of first VIA (select all relevant)	Categorical	0 = no growth 1 = trichomonas 2 = chlamydia 3 = candida 4 = Gonorrhea 5 = HSV 6 = indeterminate results 88 = other 99 = not recorded	
133	swabs3-d	Date swabs obtained	Date	YYYY-MM-DD	

Patient level screening data for women in ART programs

Please include data on **all women, 18+ years of age, entering HIV care** between the start and end dates of your survey.

Cascade step 1: Identification Baseline patient data

				(99 for any or all missing components)	
134	swabs3_c	If response to Swabs3_n = 88, describe	String		
135	swabs4	Swabs done subsequently to swabs3_d	Categorical	0 = no 1 = yes 99 = not recorded	
136	swabs4_n	STIs found on clinically obtained swabs at time of first VIA (select all relevant)	Categorical	0 = no growth 1 = trichomonas 2 = chlamydia 3 = candida 4 = Gonorrhea 5 = HSV 6 = indeterminate results 88 = other 99 = not recorded	
137	swabs4-d	Date swabs obtained	Date	YYYY-MM-DD (99 for any or all missing components)	
138	swabs4_c	If response to Swabs3_n = 88, describe	String		
139	art_tx_enrol	On ART treatment at the time of enrollment to HIV clinic	Categorical	0 = no 1 = yes 99 = not recorded	
140	art_tx_preenrol	Started ART treatment prior to enrollment in HIV clinic	Categorical	0 = no 1 = yes 99 = not recorded	
141	stage_bl	WHO HIV/AIDS Stage at entry into HIV care (baseline)	Categorical	1 = 1 2 = 2 3 = 3 4 = 4 99 = not recorded	
142	stage_bl_d	Date HIV/AIDS Stage at entry into care was assessed	Date	YYYY-MM-DD (99 for any or all missing components)	

Patient level screening data for women in ART programs

Please include data on **all women, 18+ years of age, entering HIV care** between the start and end dates of your survey.

Cascade step 1: Identification Baseline patient data

143	art_d1	Date 1 st line ART was started	Date	YYYY-MM-DD (99 for any or all missing components)	
144	art_d2	Date 2 nd line ART was started	Date	YYYY-MM-DD (99 for any or all missing components)	
145	art_d3	Date 3 rd line ART was started	Date	YYYY-MM-DD (99 for any or all missing components)	
146	vital	Last vital status	Categorical	1 = alive 2 = dead 3 = lost to follow-up 99 = not recorded	
147	cause_mort	If response to vital = 2, what was the cause of mortality	String		
148	vital_d	Date that last vital status obtained (this should be as close to data_entry_end as possible)	Date	YYYY-MM-DD (99 for any or all missing components)	

Cascade Step 2: Invited

200	invited	Woman was INVITED for screening	Numeric	1 = yes 2 = no 99 = not recorded	
201	invited_d	Date that woman was invited for screening	Date	YYYY-MM-DD	

Cascade Step: 3 Screened

300	screened	Did the woman receive cervical cancer screening	Categorical	0 = no 1 = yes 99 = not recorded	If response to screened = 0, go to cascade step 4
301	screen_via	Did the woman receive VIA screening	Categorical	0 = no	If response screen_via = 0, go to screen_pap

Cascade Step: 3 Screened					
				1 = yes 99 = not recorded	
302	via_1	VIA result visit 1	Categorical	0 = negative 1 = positive 2 = indeterminate 3 = suspicious of cancer 99 = not recorded	
303	via_1d	Date via_1 obtained	Date	YYYY-MM-DD (99 for any or all missing components)	
304	screen_pap	Did the woman receive PAP smear	Categorical	0 = no 1 = yes 99 = not recorded	If response to screen_pap = 0 , go to hpv_1
305	smear_cin_1	Smear results at visit 1, presence of neoplasia	Categorical	0 = No neoplasia +/- benign disease 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
306	smear_benign_1	Smear results at visit 1, presence of benign disease (select all relevant)	Categorical	0 = No benign disease +/- CIN 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
307	smear_1c	If response to smear_benign_1 = 88, explain smear (cytological) findings	String		
308	smear_1d	Date Smear_1 obtained	Date	YYYY-MM-DD (99 for any or all missing components)	
309	screen_hpv	Woman received HPV smear	Categorical	0 = no 1 = yes 99 = not recorded	
310	hpv_res_1	Result of HPV test at visit 1	Categorical	0 = negative 1 = positive 99 = not recorded	If response to hpv_res_1 = 0 , go to referral_screen1
311	hpv_1c	If response to HPV_1 = 1, please indicate	Numerical	Continuous variable 99 = not recorded	

Cascade Step: 3 Screened					
		the HPV sub-type (s) identified			
312	referral_screen1	Referral for second opinion VIA (both within clinic and to another clinic)	Categorical	0 = no 1 = yes 66 = unclear	If response to referral_screen1= 0, go to referral_treat1
313	referral_screen1d	Date referral_screen1 obtained	Date	YYYY-MM-DD 99 for any or all missing components)	
314	referral_treat1	Referral for treatment (both within clinic and to another clinic)	Categorical	0 = no 1 = yes 99 = not recorded	If response to referral_treat1= 0, go to via_2
315	referred_treat1d	Date referral_treat1 obtained	Date	YYYY-MM-DD 99 for any or all missing components)	
316	via_2	VIA result visit 2 (by same clinician or another clinician within same clinic OR at another clinic if second opinion required following initial VIA screening)	Categorical	0 = did not receive VIA_2 1 = positive 2 = negative 3 = indeterminate 4 = suspicious of cancer 99 = not recorded	If response to via_2 = 0, go to cascade step 4
317	via_2d	Date VIA_2 result obtained	Date	YYYY-MM-DD 99 for any or all missing components)	
318	via_2_c	Reason for via_2	String	What was the reason for a second VIA (for example, cervicitis at original visit follow-up following treatment, another opinion, biopsy)	

Cascade Step 4: Diagnosed					
400	dx_bx	Woman received diagnostic biopsy	Categorical	0 = no 1 = yes 99 = not recorded	If response to dx_bx = 0, go to cascade step 5
401	bx_d	Date biopsy obtained	Date	YYYY-MM-DD 99 for any or all missing components)	

Cascade Step 4: Diagnosed					
402	bx_cin	Biopsy result at via_1 or via_2, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
403	bx_benign	Biopsy results at via_1 or via_2, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
404	bx_c	If response to bx_benign_2= 88, describe histology findings	String		

Cascade Step 5: Treated					
500	treated	Woman received treatment for cervical cancer screening	Categorical	0 = no 1 = yes 99 = not recorded	If response to Treated = 0, go to cascade step 6
501	cryo_1	Received cryotherapy	Categorical	0 = no 1 = yes 99 = not recorded	
502	cryo_1d	Date that cryotherapy was received	Date	YYYY-MM-DD 99 for any or all missing components)	
503	leep_1	LEEP done	Categorical	0 = no 1 = yes 99 = not recorded	
504	leep_1d	Date of LEEP	Date	YYYY-MM-DD	
505	leep_cin_1	Histology results from leep_1, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
506	leep_benign_1	Histology results from leep_1, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
507	leep_1c	If response to leep_benign_1= 88, please describe histological findings	String		

Cascade Step 6: Follow-up 1					
600	fu	Did woman receive first follow-up visit (fu1)	Categorical	0 = no 1 = yes 99 = not recorded	If response to fu = 0, go to cascade step 7 "Cancer"

Cascade Step 6: Follow-up 1					
601	screenby_fu1	Person performing first follow-up	Categorical	1 = nurse 2 = lay health worker 3 = doctor other than gynecologist 4 = gynecologist 99 = not recorded	
602	via_fu1	Did the woman receive VIA at her first follow-up visit	Categorical	0 = no 1 = yes 99 = not recorded	If response = 0, go to smear_fu1
603	via_res_fu1	VIA result at fu1	Categorical	0 = negative 1 = positive 2 = indeterminate 3 = suspicious of cancer 99 = not recorded	In treated women, _fu1 will inform the cascade step "treatment outcomes" In all other women it will inform the cascade step "re-examine" If response via_res_fu1 = 0, go to follow-up 2
604	via_fu1_d	Date via_res_fu1 obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
605	smear_fu1	Did the woman receive a smear at fu1	Categorical	0 = no 1 = yes 99 = not recorded	If response to Smear_fu1 = 0, go to HPV_fu1
606	smear_cin_fu1	Smear results at fu1, presence of neoplasia	Categorical	0 = No neoplasia +/- benign disease 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
607	smear_benign_fu1	Smear results at fu1, presence of benign disease (select all relevant)	Categorical	0 = No benign disease +/- CIN 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
608	smear_fu1_c	If response to smear_benign_fu1 = 88, describe smear (cytological) findings	String		

Cascade Step 6: Follow-up 1					
609	smear_fu1_d	Date of smear obtained at fu1	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
610	hpv_fu1	Woman received HPV testing at follow-up	Categorical	0 = no 1 = yes 99 = not recorded	If response hpv_fu1 = 0, go to bx_fu1
611	hpv_res_fu1	Result of HPV test at fu1	Categorical	0 = negative 1 = positive 99 = not recorded	
612	hpv_fu1_c	If response to hpv_fu1 = 1, please indicate the HPV sub-type identified	Numerical	Continuous variable 99 = not reported	
613	bx_fu1	Was a biopsy done at fu1	Categorical	0 = no 1 = yes 99 = not recorded	If response to bx_fu1= 0, go to cryo_fu1
614	bx_fu1_d	Date that the biopsy from fu1 was obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
615	bx_cin_fu1	Biopsy result at fu1, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
616	bx_benign_fu1	Smear results at fu1, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
617	bx_fu1_c	If response to bx_benign_fu1 = 88, explain the histological findings	String		
618	treat_fu1	Did the woman receive treatment at fu1	Categorical	0 = no 1 = yes 99 = not recorded	

Cascade Step 6: Follow-up 1					
619	cryo_fu1	Received cryotherapy at fu1	Categorical	0 = no 1 = yes 99 = not recorded	If response to cryo_fu1 = 0, go to leap_fu1
620	cryo_fu1_d	Date that Cryo_fu1 was received	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
621	leap_fu1	LEEP done at fu1	Categorical	0 = no 1 = yes 99 = not recorded	If response to leap_fu1 = 0, go ref_fu1
622	leap_fu1_d	Date that leap_fu1 was performed	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
623	leap_cin_fu1	Histology results from leap_fu1, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
624	leap_benign_fu1	Histology results from leap_fu1, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
625	leap_fu1_c	If response to leap_benign_fu1 = 88, please describe (histological) findings	String		
626	ref_fu1	Referral made at fu1	Categorical	0 = no referral made 1 = referral for further screening 2 = referral for treatment pre-cancer 3 = referral for treatment of suspected cancer 88 = other 99 = not recorded	If response to ref_fu1 = 0, 1, 2, 88, 99, go to follow-up 2 If response to ref_fu1 = 3, go to Cascade step 8
627	ref_fu1c	If response to ref_fu1 = 88, please explain	String		
628	ref_date_fu1	Date referral at follow-up 1 obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	

Follow-up2					
700	fu	Did woman receive second follow-up visit (fu2)	Categorical	0 = no 1 = yes 99 = not recorded	If response to fu = 0, go to cascade step 7 "Cancer"
701	screenby_fu2	Person performing second follow-up	Categorical	1 = nurse 2 = lay health worker 3 = doctor other than gynecologist 4 = gynecologist 99 = not recorded	
702	via_fu2	Did the woman receive VIA at her second follow-up visit	Categorical	0 = no 1 = yes 99 = not recorded	If response = 0, go to smear_fu2
703	via_res_fu2	VIA result at fu2	Categorical	0 = negative 1 = positive 2 = indeterminate 3 = suspicious of cancer 99 = not recorded	In treated women, _fu2 will inform the cascade step "treatment outcomes" In all other women it will inform the cascade step "re-examine" If response via_res_fu2 = 0, go to follow-up 2
704	via_fu2_d	Date via_res_fu2 obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
705	smear_fu2	Did the woman receive a smear at fu2	Categorical	0 = no 1 = yes 99 = not recorded	If response to Smear_fu2 = 0, go to HPV_fu2
706	smear_cin_fu2	Smear results at fu2, presence of neoplasia	Categorical	0 = No neoplasia +/- benign disease 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	

Follow-up2					
707	smear_benign_fu2	Smear results at fu2, presence of benign disease (select all relevant)	Categorical	0 = No benign disease +/- CIN 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
708	smear_fu2_c	If response to smear_benign_fu2 = 88, describe smear (cytological) findings	String		
709	smear_fu2_d	Date of smear obtained at fu2	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
710	hpv_fu2	Woman received HPV testing at follow-up	Categorical	0 = no 1 = yes 99 = not recorded	If response hpv_fu2 = 0, go to bx_fu2
711	hpv_res_fu2	Result of HPV test at fu2	Categorical	0 = negative 1 = positive 99 = not recorded	
712	hpv_fu2_c	If response to hpv_fu2 = 1, please indicate the HPV sub-type identified	Numerical	Continuous variable 99 = not reported	
713	bx_fu2	Was a biopsy done at fu2	Categorical	0 = no 1 = yes 99 = not recorded	If response to bx_fu2= 0, go to cryo_fu2
714	bx_fu2_d	Date that the biopsy from fu2 was obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
715	bx_cin_fu2	Biopsy result at fu2, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
716	bx_benign_fu2	Smear results at fu2, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	

Follow-up2					
717	bx_fu2_c	If response to bx_benign_fu2 = 88, explain the histological findings	String		
718	treat_fu2	Did the woman receive treatment at fu2	Categorical	0 = no 1 = yes 99 = not recorded	
719	cryo_fu2	Received cryotherapy at fu2	Categorical	0 = no 1 = yes 99 = not recorded	If response to cryo_fu2 = 0, go to leap_fu2
720	cryo_fu2_d	Date that Cryo_fu2 was received	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
721	leap_fu2	LEEP done at fu2	Categorical	0 = no 1 = yes 99 = not recorded	If response to leap_fu2 = 0, go ref_fu2
722	leap_fu2_d	Date that leap_fu2 was performed	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
723	leap_cin_fu2	Histology results from leap_fu2, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
724	leap_benign_fu2	Histology results from leap_fu2, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
725	leap_fu2_c	If response to leap_benign_fu2 = 88, please describe (histological) findings	String		

Follow-up2					
726	ref_fu2	Referral made at fu2	Categorical	0 = no referral made 1 = referral for further screening 2 = referral for treatment precancer 3 = referral for treatment of suspected cancer 88 = other 99 = not recorded	If response to ref_fu2 = 0, 1, 2, 88, 99, go to follow-up 2 If response to ref_fu2 = 3, go to Cascade step 8
727	ref_fu2c	If response to ref_fu2 = 88, please explain	String		
728	ref_date_fu2	Date referral at follow-up 1 obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	

Follow-up3					
800	fu	Did woman receive third follow-up visit (fu3)	Categorical	0 = no 1 = yes 99 = not recorded	If response to fu = 0, go to cascade step 7 “Cancer”
801	screenby_fu3	Person performing third follow-up	Categorical	1 = nurse 2 = lay health worker 3 = doctor other than gynecologist 4 = gynecologist 99 = not recorded	
802	via_fu3	Did the woman receive VIA at her third follow-up visit	Categorical	0 = no 1 = yes 99 = not recorded	If response = 0, go to smear_fu3
803	via_res_fu3	VIA result at fu3	Categorical	0 = negative 1 = positive 2 = indeterminate 3 = suspicious of cancer 99 = not recorded	In treated women, _fu3 will inform the cascade step “treatment outcomes” In all other women it will inform the cascade step “re-examine” If response via_res_fu3 = 0, go to follow-up 2

Follow-up3					
804	via_fu3_d	Date via_res_fu3 obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
805	smear_fu3	Did the woman receive a smear at fu3	Categorical	0 = no 1 = yes 99 = not recorded	If response to Smear_fu3 = 0, go to HPV_fu3
806	smear_cin_fu3	Smear results at fu3, presence of neoplasia	Categorical	0 = No neoplasia +/- benign disease 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
807	smear_benign_fu3	Smear results at fu3, presence of benign disease (select all relevant)	Categorical	0 = No benign disease +/- CIN 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
808	smear_fu3_c	If response to smear_benign_fu3 = 88, describe smear (cytological) findings	String		
809	smear_fu3_d	Date of smear obtained at fu3	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
810	hpv_fu3	Woman received HPV testing at follow-up	Categorical	0 = no 1 = yes 99 = not recorded	If response hpv_fu3 = 0, go to bx_fu3
811	hpv_res_fu3	Result of HPV test at fu3	Categorical	0 = negative 1 = positive 99 = not recorded	
812	hpv_fu3_c	If response to hpv_fu3 = 1, please indicate the HPV sub-type identified	Numerical	Continuous variable 99 = not reported	
813	bx_fu3	Was a biopsy done at fu3	Categorical	0 = no 1 = yes 99 = not recorded	If response to bx_fu3= 0, go to cryo_fu3

Follow-up3					
814	bx_fu3_d	Date that the biopsy from fu3 was obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
815	bx_cin_fu3	Biopsy result at fu3, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
816	bx_benign_fu3	Smear results at fu3, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
817	bx_fu3_c	If response to bx_benign_fu3 = 88, explain the histological findings	String		
818	treat_fu3	Did the woman receive treatment at fu3	Categorical	0 = no 1 = yes 99 = not recorded	
819	cryo_fu3	Received cryotherapy at fu3	Categorical	0 = no 1 = yes 99 = not recorded	If response to cryo_fu3 = 0, go to leap_fu3
820	cryo_fu3_d	Date that Cryo_fu3 was received	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
821	leap_fu3	LEEP done at fu3	Categorical	0 = no 1 = yes 99 = not recorded	If response to leap_fu3 = 0, go ref_fu3
822	leap_fu3_d	Date that leap_fu3 was performed	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
823	leap_cin_fu3	Histology results from leap_fu3, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	

Follow-up3					
824	leep_benign_fu3	Histology results from leep_fu3, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
825	leep_fu3_c	If response to leep_benign_fu3 = 88, please describe (histological) findings	String		
826	ref_fu3	Referral made at fu3	Categorical	0 = no referral made 1 = referral for further screening 2 = referral for treatment precancer 3 = referral for treatment of suspected cancer 88 = other 99 = not recorded	If response to ref_fu3 = 0, 1, 2, 88, 99, go to follow-up 2 If response to ref_fu3 = 3, go to Cascade step 8
827	ref_fu3	If response to ref_fu3 = 88, please explain	String		
828	ref_date_fu3	Date referral at follow-up 1 obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	

Follow-up4					
900	fu	Did woman receive fourth follow-up visit (fu4)	Categorical	0 = no 1 = yes 99 = not recorded	If response to fu = 0, go to cascade step 7 “Cancer”
901	screenby_fu4	Person performing fourth follow-up	Categorical	1 = nurse 2 = lay health worker 3 = doctor other than gynecologist 4 = gynecologist 99 = not recorded	
902	via_fu4	Did the woman receive VIA at her fourth follow-up visit	Categorical	0 = no 1 = yes 99 = not recorded	If response = 0, go to smear_fu4

Follow-up4					
903	via_res_fu4	VIA result at fu4	Categorical	0 = negative 1 = positive 2 = indeterminate 3 = suspicious of cancer 99 = not recorded	In treated women, _fu4 will inform the cascade step “treatment outcomes” In all other women it will inform the cascade step “re-examine” If response via_res_fu4 = 0, go to follow-up 2
904	via_fu4_d	Date via_res_fu4 obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
905	smear_fu4	Did the woman receive a smear at fu4	Categorical	0 = no 1 = yes 99 = not recorded	If response to Smear_fu4 = 0, go to HPV_fu4
906	smear_cin_fu4	Smear results at fu4, presence of neoplasia	Categorical	0 = No neoplasia +/- benign disease 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
907	smear_benign_fu4	Smear results at fu4, presence of benign disease (select all relevant)	Categorical	0 = No benign disease +/- CIN 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
908	smear_fu4_c	If response to smear_benign_fu4 = 88, describe smear (cytological) findings	String		
909	smear_fu4_d	Date of smear obtained at fu4	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
910	hpv_fu4	Woman received HPV testing at follow-up	Categorical	0 = no 1 = yes 99 = not recorded	If response hpv_fu4 = 0, go to bx_fu4
911	hpv_res_fu4	Result of HPV test at fu4	Categorical	0 = negative 1 = positive 99 = not recorded	

Follow-up4					
912	hpv_fu4_c	If response to hpv_fu4 = 1, please indicate the HPV sub-type identified	Numerical	Continuous variable 99 = not reported	
913	bx_fu4	Was a biopsy done at fu4	Categorical	0 = no 1 = yes 99 = not recorded	If response to bx_fu4= 0, go to cryo_fu4
914	bx_fu4_d	Date that the biopsy from fu4 was obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
915	bx_cin_fu4	Biopsy result at fu4, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
916	bx_benign_fu4	Smear results at fu4, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
917	bx_fu4_c	If response to bx_benign_fu4 = 88, explain the histological findings	String		
918	treat_fu4	Did the woman receive treatment at fu4	Categorical	0 = no 1 = yes 99 = not recorded	
919	cryo_fu4	Received cryotherapy at fu4	Categorical	0 = no 1 = yes 99 = not recorded	If response to cryo_fu4 = 0, go to leap_fu4
920	cryo_fu4_d	Date that Cryo_fu4 was received	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
921	leap_fu4	LEEP done at fu4	Categorical	0 = no 1 = yes 99 = not recorded	If response to leap_fu4 = 0, go ref_fu4

Follow-up4					
922	leep_fu4_d	Date that leep_fu4 was performed	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
923	leep_cin_fu4	Histology results from leep_fu4, presence of neoplasia	Categorical	0 = No neoplasia 1 = CIN1 2 = CIN2 3 = CIN3 4 = ICC 5 = ASCUS 99 = not recorded	
924	leep_benign_fu4	Histology results from leep_fu4, presence of benign disease (select all relevant)	Categorical	0 = No benign disease 1 = HPV 2 = cervicitis 88 = other 99 = not recorded	
925	leep_fu4_c	If response to leep_benign_fu4 = 88, please describe (histological) findings	String		
926	ref_fu4	Referral made at fu4	Categorical	0 = no referral made 1 = referral for further screening 2 = referral for treatment precancer 3 = referral for treatment of suspected cancer 88 = other 99 = not recorded	If response to ref_fu4 = 0, 1, 2, 88, 99, go to follow-up 2 If response to ref_fu4 = 3, go to Cascade step 8
927	ref_fu4	If response to ref_fu4 = 88, please explain	String		
928	ref_date_fu4	Date referral at follow-up 1 obtained	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	

Cascade Step 7: Cancer					
1000	cancer	Woman has developed cervical cancer during study period	Categorical	1 = yes 2 = no 99 = not recorded	
1001	cx_treat_eua	Did the woman receive and examination under anesthesia (EUA)	Categorical	1 = yes 2 = no 99 = not recorded	
1002	cx_treat_eua_d	Date of EUA	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
1003	cx_treat_cone	Did the woman receive a cone biopsy	Categorical	1 = yes 2 = no 99 = not recorded	
1004	cx_treat_cone_d	Date of cone biopsy	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
1005	cx_treat_hyst	Did the woman receive a simple hysterectomy	Categorical	1 = yes 2 = no 99 = not recorded	
1006	cx_treat_hyst_d	Date of simple Hysterectomy	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
1007	cx_treat_radhyst	Did the woman receive a radical hysterectomy + lymph node dissection (LNs)	Categorical	1 = yes 2 = no 99 = not recorded	
1008	cx_treat_radhyst_d	Date of radical hysterectomy + lymph node dissection (LNs)	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
1009	cx_treat_rtx	Did the woman receive radiotherapy	Categorical	1 = yes 2 = no 99 = not recorded	
1010	cx_treat_rtx_d	Date of radiotherapy	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
1011	cx_treat_ctx	Did the woman receive chemotherapy	Categorical	1 = yes 2 = no 99 = not recorded	
1012	cx_treat_ctx_d	Date of chemotherapy	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	

1013	cx_treat_hosppal	Did the woman receive hospital palliation	Categorical	1 = yes 2 = no 99 = not recorded	
1014	cx_treat_hosppal_d	Date of hospital palliative therapy	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	
1015	cx_treat_homepal	Did the woman receive home palliation	Categorical	1 = yes 2 = no 99 = not recorded	
1016	cx_treat_homepal_d	Date of home palliative therapy	Date	YYYY-MM-DD (99 for any or all missing components – Y/M/D)	

Appendix 4. Flow diagram of women included in the analysis

ART: Antiretroviral Therapy; n: number of women

Appendix 5: Results of the cervical cancer prevention cascade using the longitudinal approach

Secondary cervical cancer prevention cascade	Number of women	Time to stage days, median (IQR)	Cumulative incidence at 2 years* % (95%CI)
Screening arm			
Women in care	1624	63 (28-146)	85.4 (83.5-87.1)
Screened	1385	63 (28-154)	60.6 (58.1-62.9)
Screen-negative at first screening	989	374 (361-424)	44.9 (42.3-47.3)
Rescreened	791	374 (363-427)	40.6 (38.1-43.0)
Screen-negative at rescreening	713		
Preventative treatment arm			
Screen-positive at first screening	396	64.5 (28-133)	
Treated	316	13 (0-37)	79.5 (75.1-83.2)
Rescreened	277	188 (181-223)	61.7 (56.6-66.3)
Screen-negative at rescreening	169	188 (182-231)	36.1 (31.2-40.7)

Longitudinal approach uses all individual patient level data available over the study period; *Start stage for cumulative incidence in the screening arm was the date of women's first ART clinic appointment, end stages are the indicated cascade stages occurring subsequently; [§]start stage for cumulative incidence in the preventative treatment arm is the screen-positive date at first screening, end stages are the indicated cascade stages occurring subsequently; n: number of women, IQR: inter-quartile range, CI: confidence interval

Appendix 6. Patient flow in cervical screening during the full study period

N = number of women, STI: sexually transmitted infection, HIV: human immunodeficiency virus.

Appendix 7. The preventative treatment arm, disaggregated by mode of treatment

Panel A: the number of women proceeding through the care cascade over the whole study period; Panel B: the number of women proceeding through the care cascade within guideline indicated time-frame; LEEP: Loop Electrosurgical Excision Procedure.

Appendix 8. Crude and adjusted hazard ratios for factors associated with screen-negativity after treatment

	Univariable analysis n = 1251			Multivariable analysis n = 1251		
	HR	95% CI	P value	HR	95% CI	P value
Age, years						
<25	1.13	0.65-1.96	0.216	1.26	0.65-2.48	0.075
25-44	1	-		1	-	
>45	1.78	0.87-3.62		2.33	1.03-5.26	
Relationship						
Single	0.81	0.56-1.17	0.413			
Relationship	1	-				
Separated	0.81	0.55-1.18				
Employment						
Unemployed	1	-	0.001	1	-	0.122
Employed	1.00	0.59-1.14		0.84	0.59-1.19	
Student	0.09	0.01-0.64		0.15	0.02-1.08	
Parity						
0			0.841			0.991
1 to 3	0.94	0.56-1.59		0.99	0.51-1.91	
>3	1.06	0.58-1.95		0.96	0.45-2.04	
HIV RNA viral load at VIA screening, copies/ mm³						
<50	1	-	0.275	1	-	0.546
50-1000	1.16	0.70-1.92		1.08	0.64-1.82	
>1000	1.31	0.94-1.82		1.22	0.86-1.75	
Year enrolled, year						
Early years (2012-2014)	1	-	0.533	1	-	0.316
Later years (2015-2017)	0.90	0.66-1.24		0.84	0.59-1.19	

Copies/ mm³: copies in a cubic millimetre; CI: confidence interval; HIV: human immunodeficiency virus; HR: hazards ratio; n: number of women; n: number of women; RNA: Ribonucleic acid; VIA: visual inspection with acetic acid; n: number of women.