

# Adherence to Treatment and Follow-Up of Precancerous Cervical Lesions in Ethiopia

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## Abstract

**Background:** In Ethiopia, both incidence and mortality of cervical cancer are relatively high. Screening services, which were implemented during the past few years, are currently being expanded. The World Health Organization recommends patients with a positive VIA (visual inspection with acetic acid) result should immediately receive treatment followed by rescreening after 1 year as precancerous lesions can reoccur or become residential despite treatment.

**Materials and Methods:** Screening logbooks dating between 2017 and 2020 were retrospectively reviewed in 14 health facilities of Addis Ababa and Oromia region. Data for 741 women with a VIA-positive result were extracted and those women were asked to participate in a questionnaire-based phone interview to gain insights about adherence to treatment and follow-up. Data were analyzed using descriptive methods and then fitted into 2 generalized linear models to test variables for an influence on adherence to follow up.

**Results:** Around 13 800 women had received a VIA screening, of which approximately 820 (5.9%) were VIA positive. While over 90% of women with a positive screen received treatment, only about half of the treated patients returned for a follow-up examination. After treatment, 31 women had a VIA-positive re-screen. We found that educational status, age over 40, no/incorrect follow-up appointment, health facility-related barriers, and use of reminders are important drivers of adherence to follow up.

**Conclusion:** Our results revealed that adherence to treatment after VIA positive screening is relatively high whereas adherence to follow up recommendations still needs improvement. Reminders like appointment cards and phone calls can effectively reduce the loss of follow-up.

**Key words:** cervical cancer screening; precancerous lesions; cryotherapy; follow-up; adherence; recurrence.

## Implications for Practice

This study may contribute to the development of evidence-based guidelines for the appropriate follow-up of women with abnormal cervical cancer screening results. This study emphasizes the importance of appropriate follow-up of women with abnormal cervical cancer screening results and the adherence to those. Findings from the study may have implications for health policy decisions, guideline development and resource allocation. It can inform policymakers about the necessary infrastructure, training, and equipment needed for effective follow-up after cervical cancer screening. Additionally, the study results can help to improve patient education and counseling practices and can therefore alleviate anxiety, improve patient satisfaction, and foster informed decision-making.

## Introduction

Cervical cancer (CC) is one of the most prevalent cancers in women worldwide, with a disproportionate impact on women in low- and middle-income countries.<sup>1</sup> While screening and vaccination programs in Europe and Northern America have

drastically reduced CC incidence and mortality, it is still a major health threat for women in Sub-Saharan Africa.<sup>2</sup> In Ethiopia, approximately 5000 women die of CC every year.<sup>3</sup> Higher CC mortality in Sub-Saharan Africa can be attributed to late-stage presentation, predominantly due to lack of

information and a dearth or inaccessibility of prevention services.<sup>2,4,5</sup>

The Ethiopian CC screening program was first launched in 2009 as part of the Pathfinder project which focused on women living with HIV.<sup>6</sup> The service was subsequently scaled-up until it is now offered in health facilities throughout Ethiopia and includes HIV-negative women.<sup>6,7</sup> Even though the uptake of CC screening in Ethiopia increased in recent years, the percentage of women who received at least one screening remains relatively low, at approximately 15%.<sup>8,9</sup> The first national guideline for the prevention of cervical cancer was published in 2015, currently the second edition (2021) is used.<sup>6,10</sup> The standard screening method for CC in Ethiopia is visual inspection with acetic acid (VIA).<sup>6</sup> In addition, some health facilities recently started offering HPV testing as an alternative (mainly for WLHIV). In VIA-screenings, aceto-white cervical lesions are signs of precancerous stages of cell transformation but can also be caused by inflammation of the cervix.<sup>11</sup> Depending on the size and location of the lesions, they should be treated with either cryotherapy/thermal ablation or loop electrical excision procedure (LEEP).<sup>6,11</sup> When cryotherapy/thermal ablation is used, a single-visit-approach is recommended, meaning that the patient should receive the treatment on the same day of screening.<sup>6</sup> Therefore, all health centers and hospitals performing CC screening should also be equipped to perform cryotherapy or thermal ablation.<sup>6</sup> While the *single-visit approach* is generally feasible and beneficial in low-resource settings, it is sometimes not followed due to the lack of resources such as trained health professionals, cryotherapy machines, carbon dioxide for cryotherapy, and electricity for thermal ablation.<sup>12-14</sup> Non-adherence to the *single-visit approach* increases the patients' risk of not receiving treatment.<sup>15-17</sup> One Ethiopian study reports on a project, called the *Addis Tesfa (New Hope) project*, which aimed to enhance CC screening for women living with HIV (WLHIV) between August 2010 and March 2014.<sup>15</sup> According to *Addis Tesfa (New Hope)* project report, 97% of patients with cryotherapy-eligible lesions received treatment.<sup>15</sup> Patients with lesions non-eligible for cryotherapy will usually be referred to a hospital for LEEP treatment and further diagnostic services as needed.<sup>6</sup>

In Ethiopia, CC screenings are recommended every 5 years for the general population and every 2 years for WLHIV.<sup>6</sup> All patients who received a treatment for an aceto-white lesion should come back for a follow-up examination one year after their treatment as precancerous lesions can become residual or reoccur after treatment.<sup>1,6</sup> According to the WHO guideline, ablative treatment of precancerous lesions fails in approximately 10% of cases—but reliable evidence is still lacking and a higher risk of failure in WLHIV is discussed.<sup>1,18-20</sup>

Data on the adherence to guideline recommendations after VIA-positive screenings is insufficient in Ethiopia. In the *Addis Tesfa* project, 51% of women who were VIA positive and treated with cryotherapy or LEEP adhered to follow up; with a large variation between regions, from as low as 29.8% in Addis Ababa to up to 81.1% in Tigray.<sup>15</sup> In a record-based study, only 27.9% of patients returned for their 1-year follow-up.<sup>19</sup> The Ethiopian Ministry of Health (MoH) recommends the use of an appointment calendar to identify patients who missed their rescreening.<sup>6</sup> Moreover, adherence to post-treatment follow-up is listed as a core indicator to track CC screening at the national level but is not yet routinely measured within the health facilities.<sup>6</sup>

As of now, there is no structured follow-up reminder system implemented in Ethiopia. The 2021 guideline recommends for health facilities to use an appointment calendar and provide appointment cards to every client (those cards include the patients name and date of their follow-up appointment—an example is provided in the guideline's Appendix). The guideline also encourages healthcare providers to emphasize the importance of coming back for follow-up care and recommends that clinics should designate someone to ensure that follow-up is done. For women who do not return spontaneously as advised, the guideline points out 2 options: providers can either call women or ask health extension workers and case managers to contact women directly at home. However, the guideline does not specify how those actions can be put into practice (neither does the MoH ensure the availability of phones or an attached budget in the health facilities) wherefore the calling system is not functional in most places.<sup>6</sup>

The primary objective of this study is to measure the levels of adherence to treatment and follow-up in women with a positive VIA screening as well as the recurrence rate of precancerous lesions after treatment. Unlike the *Addis Tesfa* project, our study includes both WLHIV and HIV negative women which we believe to provide a more holistic reflection of follow-up rates in routine care. In addition, the current study aimed to identify enablers and barriers to adherence to follow up that could generate evidence for the development and implementation of effective CC care interventions in Ethiopia.

## Methods

### Study Design and Setting

We employed an institution-based, retrospective study design, including health facilities in 2 Ethiopian regions (Oromia region and Addis Ababa). Addis Ababa is Ethiopia's capital with more than 3 million inhabitants, while Oromia region is the largest region in Ethiopia and thereby has a far lower population density.<sup>21</sup> For each of the objectives, the sample size was determined using a single population proportion formula, applying a 5% margin of error and 95% CI (Supplementary Table S1). To reach our aim sample size of 383 data extractions, we included 10 health centers in 4 sub-cities of Addis Ababa as well as 4 hospitals in the Oromia region (each located in a different town: Adama, Assela, Bshoftu, and Weliso). For randomization, we first randomly selected 5 out of all 11 sub-cities of Addis Ababa (Arada, Bole, Gulele, Yeka, Akaki Kaliti), then created a list with suitable health facilities within those chosen areas (inclusion criteria: provision of CC screening service since 2017 and high patient flow) and finally randomly selected the included health facilities. For Oromia region, 4 hospitals were included, which started providing screenings before 2017. All health facilities provide screening as part of the routine CC screening service offered in Ethiopia.

### Data Collection

The data collection was performed from March to May 2022 and concerned logbook entries from the time between January 2017 and December 2020. For each health facility, the total number of CC screenings per year as well as the distribution of screening results were collected. We were able to retrieve screening records for 741 women out of approximately 820

VIA-positive results, the rest of the records were lacking essential information, ie, date of screening.

A data extraction form was prepared which included name, address, phone number, age, marital status, parity, educational level, HIV status, screening date, screening result, treatment, reappointment date, and reappointment visits. All these information should ideally be available from the health facilities CC screening logbooks, where each performed CC screening has an entry. The logbooks are designed and provided by the MoH to monitor the program. Logbook entries should ideally be completed during the client's visit. One nurse from each health facility received a 1-day training and then filled out the data extraction forms. Patient files were reviewed when information was missing in the logbooks. Patient files are another place to store information, not only in regard to CC screening, within the health facilities. Their design and completeness depend on the level of use within each health facility.

For our study, patients under the age of 18 years and patients with suspected cancer lesions were not included, since the latter follow different pathways depending on further diagnostics. Two trained research assistants and one of the principal investigators digitalized the anonymized data from the hard-copy data extraction form by entering it into ODK<sup>22</sup> or REDCap (Research Electronic Data Capture).<sup>23,24</sup>

All women were invited to a questionnaire-based phone interview (Supplementary Table S2). The structured questionnaire was initially developed in English, based on related literature.<sup>25-27</sup> Questions on barriers and enablers were adapted to cover the “5 A’s” of the concept of access: availability, accessibility, accommodation, affordability, and acceptability.<sup>28</sup> Modifications to the questionnaire were made after expert discussion before it was translated to Amharic and pretested on 5% of the sample size. Minor modifications were made after the pretest to ensure clarity. The final questionnaire consisted of 5 parts including socio-demographic information (age, marital status, parity, educational level, occupation, and income), information on the treatment of precancerous cervical lesions, adherence to follow up recommendations, and questions on individual and health-facility-related barriers, and enablers for follow-up. Phone interviews were conducted with 399 women (response rate of 78.6% in Addis Ababa and 36.1% in Oromia region). Only 574 of all 741 women screened VIA-positive had documented phone numbers. All the 574 women were invited to the telephone interview, but only the 399 women were reached and participated. The remaining phone numbers were either switched off, not

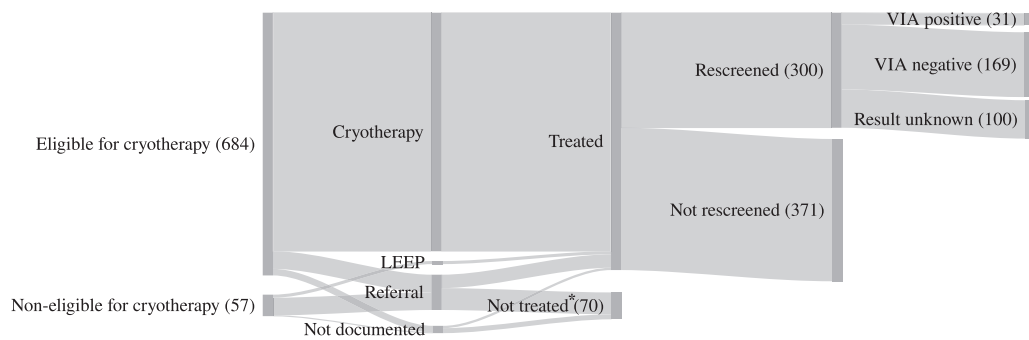
working, or out of service or not answered during repeated attempts.

### Data Analysis

Data cleaning, plotting, and statistical analyses were performed using R software.<sup>29</sup> Conversions between Ethiopian and Gregorian dates were done in Python.<sup>30</sup> Values missing in the logbook data were filled using data from the phone interviews whenever possible. The remaining cases (19 in Model<sub>1</sub>, 24 in Model<sub>2</sub>) were imputed using the variables’ median (Supplementary Table S3). Generalized linear models (binomial family) were fitted to the data to assess the possible influence of education, parity, eligibility for cryotherapy, region, marital status, HIV status, follow-up appointment, occupation, income, health facility-related barriers, individual barriers as well as the use of reminders on adherence (binary outcome). In other words, we modeled the influence of a set of explanatory variables (listed above) on the binary variable “adherence to follow up” using a logistic regression. All explanatory variables included in the models were tested a priori for collinearity and only included if  $r^2$  (squared Pearson’s correlation index) was below 0.35. In the first model, we included only variables from the logbooks, so that the model could be applied to all 671 treated patients. In a second model, information from the phone interviews was additionally considered (applied to 371 patients). The questions on barriers and enablers were grouped into health-facility-related or patient-related barriers and a score was created for each group. Each affirmed barrier added one point to the score and thus higher scores corresponded to patients facing more barriers (Supplementary Table S4). Reminders were treated as a separate explanatory variable as they portray the linkage between the healthcare system and patients and therefore depend on both sides. The Sankey plot (Fig. 1) was generated using SANKEYmatic.<sup>31</sup>

### Operational Definition of Adherence to Follow-Up

Adherence to follow up was defined as having any rescreening after the initial VIA-positive screening. Follow-up after VIA-negative screenings was not considered in this study, as it is known that women with a VIA-positive screening even after treatment have a higher risk of developing precancerous lesions. To combine the information from logbooks and phone interviews, a 2-step approach was used: First, the data extracted from the logbooks was checked for a rescreening date. Then, for those patients with no rescreening date in the



\*of those not treated, 38 were eligible for cryotherapy

Figure 1. Pathways of patients with VIA-positive CC screening.

logbook, information from the phone interviews was added, if available.

### Ethical Considerations

Ethical clearance was provided by the School of Public Health, Addis Ababa University, and the responsible health bureaus for both regions. The objective of the study was explained to all phone interview participants and their oral consent was obtained and documented.

### Results

The study sample consisted of all 741 women screened VIA-positive. This corresponds to approximately 5.4% of all 13 801 women screened in the 10 health facilities and 4 hospitals in the stated time frame.

#### Socio-Demographics Description of the Sample

The socio-demographic composition of the sample is described in Table 1. Most of the detected lesions were eligible for cryotherapy. Over 80% of the women were in the primary target age group for CC screening (30–49 years). Three-fourths (74.4%) of women were married and 65.5% had at least primary education. Most women (87.6%) had given birth with a median of 2 births per woman. In total 43.6% of our sample were WLHIV, HIV status was unknown for nearly a fifth of the sample. Occupation and income were assessed during the phone interviews, which is why this information was available for 399 women. The median (self-declared) monthly income was 3000 ETB (58.61 USD, using the exchange rate from March 1st, 2022<sup>32</sup>).

#### Pathways of Patients With a VIA-Positive Screening

The pathways of all 741 women who had a VIA-positive screening result are depicted in Fig. 1. We found logbook documentation on treatment for 630 patients. Additionally, 69 of the 111 patients without documented treatment were interviewed and 41 of these stated that they had received treatment (partly treated in other health facilities, partly not documented). Thus, 671 (90.6%) of all patients received treatment for their precancerous lesions. A total of 83% of those women with lesions eligible for cryotherapy received their treatment on the day of screening—adhering to the *single-visit approach*. Of those 134 women who did not receive the treatment on the same day, 88 received treatment within 2 weeks (median time to treatment 5 days; ranging from 1 to 227 days). Of all 92 referred patients, 38% received treatment. Additionally, 9 women reported having a negative screening at the hospital which they were referred to for treatment and therefore, did not need treatment. Of all 148 patients with cryotherapy-eligible lesions who did not adhere to the single-visit approach, 38 (25.7%) did not receive treatment at all.

A rescreening date had been documented for 203 treated patients. In addition, 97 others stated that they had received a rescreening “about a year after screening.” In total, 44.7% of the treated patients received any rescreening after the initial screening, but only 61.1% (124/203) of the rescreenings documented in the logbooks took place within 395 days after treatment. The median time between treatment and rescreening was 378 days with a range between 80 and 1714 days. In the logbooks, we found result codes for

**Table 1.** Socio-demographic and clinical characteristics of women with a positive VIA screen.

Characteristics		All women <i>n</i> = 741	Percentage	
Eligibility for cryotherapy	Yes	684	92.3	
	No	57	7.7	
Region	Addis	309	41.7	
	Oromia	432	58.3	
Age (years)	≤29	120	16.2	
	30–34	249	33.6	
	35–39	198	26.7	
	≥40	165	22.3	
	Unknown	9	1.2	
	Median (IQR)	34 (8)		
Marital status	Married	551	74.4	
	Divorced	89	12	
	Single	54	7.3	
	Widowed	38	5.1	
	Unknown	9	1.2	
Parity	0	70	9.4	
	1	168	22.7	
	2	203	27.4	
	3	117	15.8	
	>3	161	21.7	
	Unknown	22	3	
	Median	2		
Education	Illiterate	184	24.8	
	Can read and write	57	7.7	
	Primary education	218	29.4	
	Secondary education	142	19.2	
	College	125	16.9	
	Unknown	15	2	
	Median	2		
Employment <sup>1</sup>	Housewife/ unemployed	119	29.8	
	Private employee	117	29.3	
	Government employee	97	24.3	
	Daily laborer	35	8.8	
	Merchant	21	5.3	
	Other	4	1	
	Unknown	6	1.5	
	Own monthly income <sup>1</sup> (USD)	No income	40	10
		Low income (<61)	176	44.1
		Middle income (61–194)	150	37.6
High income (>194)		20	5	
Unknown		13	3.5	
Median		58.61		
HIV status	Positive	323	43.6	
	Negative	271	36.6	
	Unknown	147	19.8	

<sup>1</sup>Information only available for patients who participated in the phone interviews (*n* = 399). Values converted from ETB to USD using exchange rate from March 1st, 2022 (1 USD = 51.2 ETB).<sup>32</sup> Income categorization based on Gebremariam et al<sup>33</sup>.



200 rescreenings, of which 84.5% were VIA negative. In total, 31 women had a VIA-positive follow-up screening (13 WLHIV, 11 HIV-negative women, and 7 women with unknown HIV status). The calculated recurrence rates of precancerous lesions after treatment were 10% for WLHIV and 10.7% for women with negative or unknown HIV status.

### Factors Influencing Adherence to Follow-Up Recommendations

Figure 2 shows a forest plot with the main results of the first model including the logbook information of the 671 treated women, 300 of whom (44.7%) adhered to follow up. Compared to younger women, women aged over 40 years were more likely to adhere to follow up. Women with higher educational status adhered to the follow-up recommendation more often. In the group of re-screened women, 24.6% had no formal education, in comparison to 39.7% in the group without a rescreening. Most patients (93.7%) had received a correct follow-up appointment and those patients were more likely to adhere to follow up than their counterparts without a correct appointment date.

A forest plot with the key findings of the second model is shown in Fig. 3. In this model, all variables from logbooks and phone interviews were considered and, in comparison to Fig. 2, the effects of region, age, and follow-up appointment are not evident. The positive impact of education on adherence to follow up is still visible. Occupation and income did not show significant changes in adherence to treatment. Patients with a higher score for health facility-related barriers (*Hf-score*)

were at higher risk of loss to follow up. Concerning reminders for follow-up, 73 women reported that they did not receive any reminders, while 202 women received an appointment card and 96 received both a card and a phone call. Our model showed that both kinds of reminders drastically lowered the risk of loss to follow up.

### Discussion

This study has assessed Ethiopian women's adherence to treatment and follow-up after VIA-positive screening in Addis Ababa and Oromia region. We found an overall VIA screening positivity rate of 6.9%. Out of all 741 VIA-positive patients, 90.4% received treatment and 44.7% received a rescreening. Out of the 200 known rescreening results, 83.8% were VIA-negative. We found that age, educational level, perceived health facility barriers, and the use of reminders were associated with adherence to follow up.

### Adherence to Treatment and Single-Visit-Approach

In this study, the WHO target of a 90% treatment rate for identified cervical cancer precancerous lesions was met. This is in line with other recent studies in Ethiopia, reporting high rates of adherence to treatment.<sup>12,30</sup> The single-visit approach was followed in 83% of the cases with lesions eligible for cryotherapy/thermal ablation. In total, 88 (43.1%) of the patients who did not receive treatment the same day had been referred to other clinics, while the other patients received a recommendation to return to the same clinic for treatment. Of the referred 57 (64.8%) did not receive treatment versus

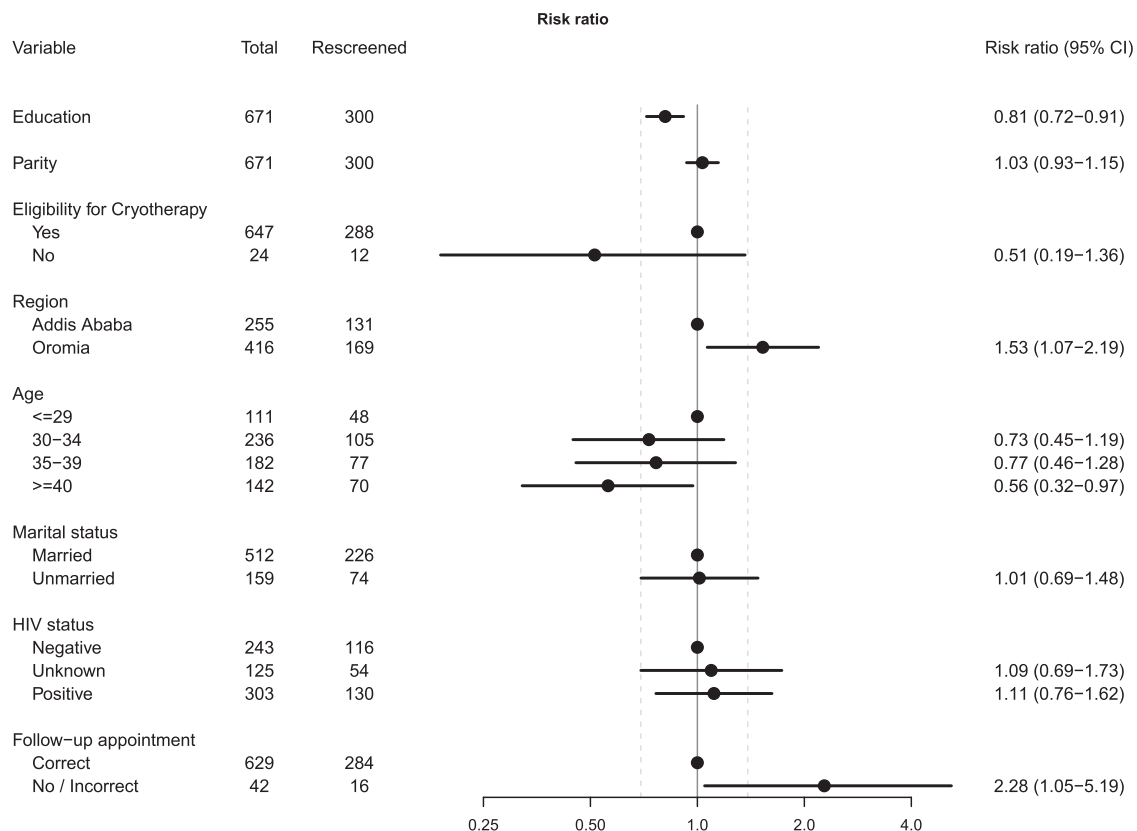
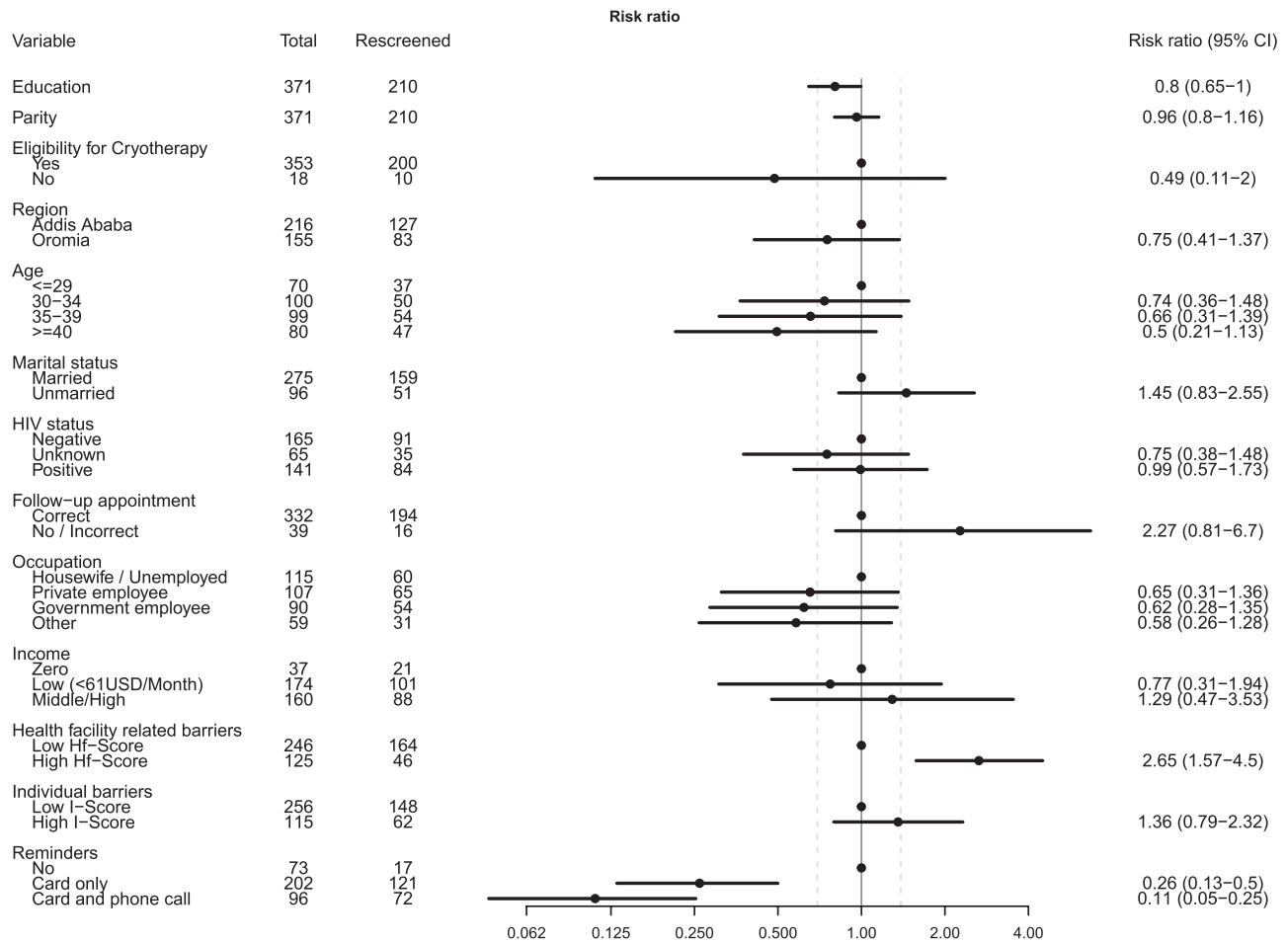


Figure 2. Forest plot showing risk ratios for non-adherence to follow-up after VIA-positive screening for factors assessed from the CC screening logbooks.



**Figure 3.** Forest plot showing risk ratios for non-adherence to follow up after VIA-positive screening for factors assessed from the CC logbooks and phone interviews with patients.

13 (11.2%) of the patients asked to come back to the same health facility. Particularly patients referred to other health facilities face access barriers—like additional transportation costs and time of travel.

Out of those cryotherapy-eligible patients who did not receive treatment the same day, 38 (25.7%) never received treatment. This is lower than the findings of a study in Côte d'Ivoire, Guyana, and Tanzania where only 52% of patients with postponed treatment returned.<sup>16</sup> Both findings stress the importance of the *single-visit approach* to minimize patients' risk of not receiving treatment. However, for those patients who managed to return for treatment, we found that delay was usually short (median of 5 days). Adherence to post-treatment recommendations like abstinence from sexual intercourse as well as treatment complications were not assessed in our study.

### Adherence to Follow-Up and Recurrence of Pre-Cancerous Lesions

The level of adherence to follow up found in our study (44.7%) is higher than purely record-based findings from 2 hospitals in Addis Ababa<sup>19</sup> and comparable to those from the Addis Tesfa project.<sup>15</sup> This is encouraging since our assessment evaluated everyday service functionality rather than project-based follow-up.

The timing of the follow-up was not included in our definition of adherence to follow up, even though it is important

to the process. Early rescreenings give health professionals the chance to monitor their patients more closely. However, more examinations are required as lesions can reoccur more than 6 months after treatment. Nevertheless, some health facilities opt for 6-month follow-up appointments (especially for WLHIV). On the other hand, late rescreening's bear the risk of further progress of the lesions with the need for more radical treatments. Still, the WHO stresses that the best time for follow-up has yet to be verified by further studies.<sup>1</sup> In this study, 0.9% of treated patients received wrong re-appointments (up to 5 years after screening) and 5.4% were not reappointed at all. To ensure that health professionals are aware of the follow-up recommendations in the guidelines, it is crucial to address the lack of access to the guidelines in many CC screening facilities as revealed in the last SARA assessment.<sup>12</sup>

We found an overall recurrence rate of (10.4%), which is lower than the 15.7% published previously for Addis Ababa.<sup>19</sup> On the other side, our findings agree with the results of a study in Harar, Eastern Ethiopia<sup>34</sup> as well as the 10% recurrence rate that the WHO estimates for the general population after treatment.<sup>1</sup>

### Factors Influencing Adherence to Follow-Up

Our study identified women's education as an important factor influencing adherence to follow up: higher education corresponded to higher likelihood of follow-up adherence.

Other studies have shown a relationship between CC screening uptake and education, with illiterate women facing higher barriers to accessing the healthcare system.<sup>5,6,9,27,35</sup> Educational status may impact health literacy, financial status, financial independence, occupation, and household responsibilities as well as traditional gender roles and sexual autonomy.<sup>9,36-38</sup> In a qualitative study from Kenya, health professionals perceived “lack of knowledge” as the most important barrier toward the treatment of precancerous lesions.<sup>39</sup> In our study, women aged over 40 years were more likely to adhere to follow up than younger women. This trend has already been shown by other studies, in which lower CC risk perception and higher stress levels in younger patients were mentioned as underlying reasons for their higher risk of non-adherence to CC screening recommendations.<sup>38,40</sup>

The *Hf-Score*, including health facility-related barriers to follow up screenings such as lack of counseling and long waiting times (Supplementary Table S5), revealed an influence on adherence to follow up: higher scores correspond to a higher risk of non-adherence. Several studies have discussed health-facility-related barriers and how to overcome them.<sup>25-27,41,42</sup> The health-facility-related barrier reported the most—by 131 (35.3%) patients (adherent and non-adherent to follow up) was “having to wait in the health facility for a medium/long time” (compare Supplementary Table S4). In the group of women non-adherent to follow up 55 (34.2%) said that they did not receive counseling about the follow-up from the healthcare provider vs 17 (8.1%) in the group of women adherent to follow up. This highlights the need for adequate counseling during the initial visit.

A significant effect of the individual barriers score could not be shown in our study. The individual barrier mentioned most frequently by our study participants (184 times) was “Fearing an adverse outcome of the follow-up screening” such as advancement of the lesion or treatment failure. Fear has repeatedly been mentioned as one of the major barriers to the uptake of screening.<sup>43,44</sup> Interestingly, in our sample, 133 (63.3%) of all women adherent to follow up reported fearing an adverse outcome of the screening compared to only 51 (31.7%) of those non-adherent to follow up. This suggests that fear of the advancement of the disease could also work as a motivator to attend follow-ups. One might also speculate that some fears can decrease after a positive CC screening experience and therefore have a lesser impact on adherence to follow up. Distance between home and health facility proved difficult to assess as many patients could not answer the question and not all entries seem plausible. We recommend a qualitative approach to gain insight into those barriers and enablers.

In our study, marital status and parity did not influence the risk of loss to follow up. Other studies have previously suggested the influence of male partners on adherence to post-treatment recommendations both in a supporting and hindering way.<sup>39</sup> Based on the research on uptake of CC screening it is likely that involvement and education of male community members will benefit women in all steps of their CC screening.<sup>45,46</sup> In our sample 149 (40.2%) stated that their partners were supportive of the CC screening and follow-up, while only 11 women (3%) reported that their partners denied support for CC screening.

The prevalence of HIV in our sample was very high (43.6%) in comparison to the HIV prevalence of Ethiopia’s

general population (1.2% for women between 15 and 49 years; up to 3.6% for women living in urban areas).<sup>21</sup> This can be explained as CC screening programs were initially targeting WLHIV,<sup>6</sup> as they are at higher risk of developing cancer. When those programs were opened for HIV-negative women, they often remained linked to HIV clinics. HIV has not shown to have a significant impact on adherence to follow up in our study, but as the HIV rates greatly vary between different health facilities and other unknown variables that could impact these results, adherence rates might be different in a sample of patients with HIV rates at the population level.

The follow-up adherence varies between the 2 regions included in our study. This difference could be for one, the levels of health facilities included were not the same: hospitals in the Oromia region vs primary health centers in Addis Ababa. Second, the telephone response rate was much higher in Addis Ababa than in Oromia region. Finally, the socio-demographic aspects of the regions vary.<sup>21</sup> All this makes it difficult to interpret the differences in adherence to follow up between Oromia region and Addis Ababa. The *Addis Tesfa* project had shown a variation of adherence to follow up screenings between regions, with a higher level of adherence to follow up in Oromia region than in Addis Ababa.<sup>15</sup>

### Reminder Systems as Enablers to Adherence to Follow-Up Screenings

Most interviewed women (298/371) received a reminder card and 96 received additional phone calls. Interestingly, 29% of WLHIV received reminder calls vs 25.4% of HIV unknown/negative women—therefore, we can conclude that the call-based reminder system has already been partially implemented for both women with and without HIV. Experiences with reminder systems show that text messages as well as phone calls can successfully increase adherence to follow up in low-resource settings.<sup>47-50</sup> In a study from Nigeria, only about half of the women could be reached via phone, even though phone numbers were registered for nearly all of them.<sup>49</sup> In the health facilities included in our study we experienced that often phone numbers are not registered for every client. Implementing an evidence-based patient reminder system is likely to improve adherence to follow up and phone-based systems carry a great potential, as the availability of phones increases, but consistent registration of patients in need of follow-up and their contact details are the basic requirements for this.

A difficulty in the interpretation of the impact of reminders in our study is, that we did not assess whether the phone call was made before or after the follow-up appointment. In case reminder calls were made only for those who had already missed their reappointment date, their efficacy might be even higher than shown in our model.

### Strengths and Limitations

This study assesses levels of adherence in Addis Ababa and Oromia region and can be used as a baseline when measuring adherence to treatment and follow-up after CC screening over time. The large sample size and inclusion of various health facilities provide a solid basis. However, we were not able to retrieve records of all 820 VIA-positive women, which might enhance the adherence rates measured in our study, as patients with incomplete records might be less likely to

have received appropriate treatment and follow-up. The used definition of adherence to treatment and follow-up combines information from phone interviews and logbooks. While the registration in the logbooks might underestimate the adherence rates (by a lack of documentation or treatment/rescreening in other health facilities or not finding documented data during data extraction), phone interviews might tend to overestimate adherence rates due to social desirability and recall bias. We tried to minimize both biases by asking precise questions and assuring that interviewees were aware that the interviewer was not part of the health facility's team. We believe that our approach to relying on the logbooks as the primary source of information and adding information gathered in the phone interviews strengthens the reliability of our estimated adherence rates.

A selection bias applies to the interviewed women as the phone interviews could only be led with those women with access to a functional phone and a correctly registered phone number. This bias would particularly affect the number of women who received reminder phone calls in our sample, as those women whom we could not reach most likely also could not be reached by health professionals when making reminder calls. Since the lack of phone contact between the healthcare system and the patient is part of the actual scenario, we assume that our phone interview response rates reflect this issue.

## Conclusions

Adherence to treatment and follow-up after positive screens is essential to reach the overall prevention goal of reducing the incidence and mortality of CC. While our study has shown that treatment services already work well, with a high rate of adherence to the *single-visit approach*, adherence to follow up still needs to improve. It was shown that many of the well-studied barriers to the uptake of CC screening also negatively affect the adherence to follow up recommendations. We welcome the addition of adherence to treatment and follow-up as key indicators of quality of screening programs in the official monitoring. We also recommend prospective studies into modifiable factors to increase adherence to follow up, as well as implementation research improving or establishing patient reminder systems.

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## Conflict of Interest

The authors indicated no financial relationships.

## Author Contributions

Conception/design: C.Y.S., M.G., R.A., A.W., F.R., A.A., E.J.K. Provision of study material or patients: C.Y.S., M.G., R.A., A.W. Collection and/or assembly of data: C.Y.S., R.A. Data analysis and interpretation: C.Y.S., M.G., R.A., A.W., F.R., P.S., E.J.K. Manuscript writing: C.Y.S., M.G., R.A., A.W., F.R., B.M., B.T.M., E.J.K. Final approval of manuscript: All authors.

## Data Availability

The data underlying this article cannot be shared publicly due to the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

## Supplementary Material

Supplementary material is available at *The Oncologist* online.

## References

- World Health Organization. *WHO Guideline for Screening and Treatment of Cervical Pre-cancer Lesions for Cervical Cancer Prevention*. 2nd ed. Geneva: WHO. 2021.
- Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-249. <https://doi.org/10.3322/caac.21660>
- World Health Organization. *Cervical Cancer country profiles – ETHIOPIA*. 2021. Accessed February 26, 2023. <https://www.who.int/teams/noncommunicable-diseases/surveillance/data/cervical-cancer-profiles>
- Bruni L, Serrano B, Roura E, et al. Cervical cancer screening programmes and age-specific coverage estimates for 202 countries and territories worldwide: a review and synthetic analysis. *Lancet Global Health*. 2022;10(8):e1115-e1127. [https://doi.org/10.1016/S2214-109X\(22\)00241-8](https://doi.org/10.1016/S2214-109X(22)00241-8)
- Yimer NB, Mohammed MA, Solomon K, et al. Cervical cancer screening uptake in Sub-Saharan Africa: a systematic review and meta-analysis. *Public Health*. 2021;195:105-111. <https://doi.org/10.1016/j.puhe.2021.04.014>
- Federal democratic republic of Ethiopia. Ministry of Health (2021) Guideline for Cervical Cancer Prevention and Control in Ethiopia
- Go Further Factsheet Ethiopia. 2022. Accessed December 6, 2023. <https://www.state.gov/go-further-country-fact-sheets/>
- Ayenew AA, Zewdu BF, Nigussie AA. Uptake of cervical cancer screening service and associated factors among age-eligible women in Ethiopia: systematic review and meta-analysis. *Infect Agent Cancer*. 2020;15(1):67. <https://doi.org/10.1186/s13027-020-00334-3>
- Desta M, Getaneh T, Yeserah B, et al. Cervical cancer screening utilization and predictors among eligible women in Ethiopia: a systematic review and meta-analysis. *PLoS One*. 2021;16(11):e0259339. <https://doi.org/10.1371/journal.pone.0259339>
- Federal democratic republic of Ethiopia. Ministry of Health (2015) Guideline for Cervical Cancer Prevention and Control in Ethiopia. Accessed December 6, 2023. <https://www.iccp-portal.org/resources-search>
- Mittal S, Basu P, Lucas E. Atlas of Visual Inspection of the Cervix With Acetic Acid for Screening, Triage, and Assessment for Treatment. 2020. Accessed February 26, 2023. <https://screening.iarc.fr/atlasvia.php>
- Wasiyhun T, Beyene MG, Deghebo AD, et al. Availability and readiness of cervical cancer screening service at health facilities in Ethiopia. *Ethiop J Public Health Nutr*. 2021;4(2):141-145. Accessed December 6, 2023. <https://ejphn.ephi.gov.et/index.php/ejphn/article/view/87>



13. Cremer ML, Conzuelo-Rodriguez G, Cherniak W, Randall T. Ablative therapies for cervical intraepithelial neoplasia in low-resource settings: findings and key questions. *J Glob Oncol*. 2018;4:1-10. <https://doi.org/10.1200/JGO.18.00093>
14. Lott BE, Halkiyi A, Kassa DW, et al. Health workers' perspectives on barriers and facilitators to implementing a new national cervical cancer screening program in Ethiopia. *BMC Womens Health*. 2021;21(1):185. <https://doi.org/10.1186/s12905-021-01331-3>
15. Shiferaw N, Salvador-Davila G, Kassahun K, et al. The single-visit approach as a cervical cancer prevention strategy among women with HIV in Ethiopia: successes and lessons learned. *Glob Health Sci Pract*. 2016;4(1):87-98. <https://doi.org/10.9745/GHSP-D-15-00325>
16. Anderson J, Wysong M, Estep D, et al. Evaluation of cervical cancer screening programs in Côte d'Ivoire, Guyana, and Tanzania: effect of HIV status. *PLoS One*. 2015;10(9):e0139242. <https://doi.org/10.1371/journal.pone.0139242>
17. Li ZG, Qian DY, Cen JM, Chen GD, Shu YH. Three-step versus "see-and-treat" approach in women with high-grade squamous intraepithelial lesions in a low-resource country. *Int J Gynaecol Obstet*. 2009;106(3):202-205. <https://doi.org/10.1016/j.ijgo.2009.04.011>
18. Debeaudrap P, Sobngwi J, Tebeu P-M, Clifford GM. Residual or recurrent precancerous lesions after treatment of cervical lesions in human immunodeficiency virus-infected women: a systematic review and meta-analysis of treatment failure. *Clin Infect Dis*. 2019;69(9):1555-1565. <https://doi.org/10.1093/cid/ciy1123>
19. Bogale AL, Teklehaymanot T, Ali JH, Kassie GM, Medhin G. The recurrence of cervical precancerous lesion among HIV positive and negative Ethiopian women after cryotherapy: a retrospective cohort study. *Cancer Control*. 2022;29:10732748221129708. <https://doi.org/10.1177/10732748221129708>
20. Fouw M de, Oosting RM, Rutgrink A, et al. A systematic review and meta-analysis of thermal coagulation compared with cryotherapy to treat precancerous cervical lesions in low- and middle-income countries. *Int J Gynaecol Obstet*. 2019;147(1):4-18. <https://doi.org/10.1002/ijgo.12904>
21. Central Statistic Agency (CSA) [Ethiopia] and ICF. Ethiopia Demographic and Health Survey 2016, Addis Ababa, Ethiopia, and Rockville, Maryland, USA. 2016. Accessed December 6, 2023. <https://dhsprogram.com/pubs/pdf/FR328/FR328.pdf>
22. Hartung C, Lerer A, Anokwa Y, Tseng C, Brunette W, Borriello G. Open data kit. In: Unwin T, Kleine D, Toyama K. Proceedings of the 4th ACM/IEEE International Conference on Information and Communication Technologies and Development. ICTD '10: International Conference on Information and Communication Technologies and Development. London United Kingdom, 13-12-2010 to 16-12-2010. New York, NY, USA: ACM, S. 2010; 1-12.
23. Harris PA, Taylor R, Minor BL, et al; REDCap Consortium. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform*. 2019;95:103208. <https://doi.org/10.1016/j.jbi.2019.103208>
24. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381. <https://doi.org/10.1016/j.jbi.2008.08.010>
25. Manga S, Kiyang E, DeMarco RF. Barriers and facilitators of follow-up among women with precancerous lesions of the cervix in Cameroon: a qualitative pilot study. *Int J Womens Health*. 2019;11:229-239. <https://doi.org/10.2147/IJWH.S196112>
26. Jeong SJ, Saroha E, Knight J, Roofe M, Jolly PE. Determinants of adequate follow-up of an abnormal Papanicolaou result among Jamaican women in Portland, Jamaica. *Cancer Epidemiol*. 2011;35(2):211-216. <https://doi.org/10.1016/j.canep.2010.07.004>
27. Khanna N, Phillips MD. Adherence to care plan in women with abnormal Papanicolaou smears: a review of barriers and interventions. *J Am Board Fam Pract*. 2001;14(2):123-130.
28. Penchansky R, Thomas JW. The concept of access: definition and relationship to consumer satisfaction. *Med Care*. 1981;19(2):127-140. <https://doi.org/10.1097/00005650-198102000-00001>
29. R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical; 2021
30. Python Software Foundation. Accessed December 6, 2023. <https://www.python.org/>
31. SankeyMATIC. Accessed December 6, 2023. <https://sankeymatic.com/>
32. Historical currency converter: ETB to USD. 2022. Accessed December 6, 2023. <https://fxtop.com/en/historical-currency-converter.php>
33. Gebremariam A, Assefa M, Addissie A, et al. Delayed initiation of adjuvant chemotherapy among women with breast cancer in Addis Ababa, Ethiopia. *Breast Cancer Res Treat*. 2021;187(3):877-882. <https://doi.org/10.1007/s10549-021-06131-9>
34. Wakwoya EB, Gemechu KS. Prevalence of abnormal cervical lesions and associated factors among women in Harar, Eastern Ethiopia. *Cancer Manag Res*. 2020;12:12429-12437. <https://doi.org/10.2147/CMAR.S279712>
35. Ezechi OC, Petterson KO, Gbajabiamila TA, et al. Predictors of default from follow-up care in a cervical cancer screening program using direct visual inspection in south-western Nigeria. *BMC Health Serv Res*. 2014;14:143. <https://doi.org/10.1186/1472-6963-14-143>
36. Midaksa M, Destaw A, Addissie A, Kantelhardt EJ, Gizaw M. Women's sexual autonomy as a determinant of cervical cancer screening uptake in Addis Ababa, Ethiopia: a case-control study. *BMC Womens Health*. 2022;22(1):236. <https://doi.org/10.1186/s12905-022-01829-4>
37. Oh JH. Educational expansion and health disparities in Ethiopia, 2005–2016. *Soc Sci Med*. 2019;235:112316. <https://doi.org/10.1016/j.socscimed.2019.05.021>
38. Hui S-KA, Miller SM, Wen K-Y, et al. Psychosocial barriers to follow-up adherence after an abnormal cervical cytology test result among low-income, inner-city women. *J Prim Care Community Health*. 2014;5(4):234-241. <https://doi.org/10.1177/2150131914529307>
39. Chapola J, Lee F, Bula A, et al. Barriers to follow-up after an abnormal cervical cancer screening result and the role of male partners: a qualitative study. *BMJ Open*. 2021;11(9):e049901. <https://doi.org/10.1136/bmjopen-2021-049901>
40. Peterson NB, Han J, Freund KM. Inadequate follow-up for abnormal Pap smears in an urban population. *J Natl Med Assoc*. 2003;95(9):825-832.
41. Paolino M, Arrossi S. Análisis de los motivos del abandono del proceso de seguimiento y tratamiento por parte de mujeres con lesiones precursoras de cáncer de cuello uterino en la provincia de Jujuy: implicancias para la gestión (Analysis of the reasons for abandoning the follow-up and treatment process in women with pre-cancerous cervical lesions in the province of Jujuy: implications for health management). *Salud Colect*. 2012;8(3):247-261. <https://doi.org/10.18294/sc.2012.165>
42. Lim JNW, Ojo AA. Barriers to utilisation of cervical cancer screening in Sub Sahara Africa: a systematic review. *Eur J Cancer Care (Engl)*. 2017;26(1):e12444. <https://doi.org/10.1111/ecc.12444>
43. Woldetsadik AB, Amhare AF, Bitew ST, et al. Socio-demographic characteristics and associated factors influencing cervical cancer screening among women attending in St. Paul's Teaching and Referral Hospital, Ethiopia. *BMC Womens Health*. 2020;20(1):70. <https://doi.org/10.1186/s12905-020-00927-5>
44. Brandt T, Wubneh SB, Handebo S, et al. Genital self-sampling for HPV-based cervical cancer screening: a qualitative study of preferences and barriers in rural Ethiopia. *BMC Public Health*. 2019;19(1):1026. <https://doi.org/10.1186/s12889-019-7354-4>
45. Binka C, Doku DT, Nyarko SH, Awusabo-Asare K. Male support for cervical cancer screening and treatment in rural Ghana. *PLoS One*. 2019;14(11):e0224692. <https://doi.org/10.1371/journal.pone.0224692>

46. Munthali AC, Ngwira BM, Taulo F. Exploring barriers to the delivery of cervical cancer screening and early treatment services in Malawi: some views from service providers. *Patient Prefer Adherence*. 2015;9:501-508. <https://doi.org/10.2147/PPA.S69286>
47. Thomson KA, Sandoval M, Bain C, et al. Recall efforts successfully increase follow-up for cervical cancer screening among women with human papillomavirus in Honduras. *Glob Health Sci Pract*. 2020;8(2):290-299. <https://doi.org/10.9745/GHSP-D-19-00404>
48. Mabachi NM, Wexler C, Acharya H, et al. Piloting a systems level intervention to improve cervical cancer screening, treatment and follow up in Kenya. *Front Med (Lausanne)* 2022;9:930462. <https://doi.org/10.3389/fmed.2022.930462>
49. Nwankwo TO, Okoro SO, Ukekwe FI, Ajah LO, Ozumba BC. Cervical cancer screening, adherence to and challenges of follow-up in resources poor setting. *OJPM* 2019;09(09):105-114. <https://doi.org/10.4236/ojpm.2019.99010>
50. Abdul Rashid RM, Mohamed M, Hamid ZA, Dahlui M. Is the phone call the most effective method for recall in cervical cancer screening?—results from a randomised control trial. *Asian Pac J Cancer Prev*. 2013;14(10):5901-5904. <https://doi.org/10.7314/apjcp.2013.14.10.5901>