ELSEVIER

Contents lists available at ScienceDirect

# **Gynecologic Oncology Reports**

journal homepage: www.elsevier.com/locate/gynor



# Impact of telephone reminders on posttreatment follow-up among women treated for cervical precancers in Cameroon: A randomized controlled trial

Joseph F. Nkfusai <sup>a</sup>, Simon M. Manga <sup>b,c</sup>, Kathleen Nulah <sup>b</sup>, Calvin Ngalla <sup>b</sup>, Claude Ngwayu <sup>e</sup>, Charlotte B. Mbuwir <sup>a</sup>, Nicholas Tendongfor <sup>a</sup>, Edie Gregory Halle Ekane <sup>d</sup>, Joël Fokom Domgue <sup>b,f,g,h,\*</sup>

- <sup>a</sup> Department of Public Health and Hygiene, Faculty of Health Sciences, University of Buea, Cameroon
- <sup>b</sup> Women's Health Program, Cameroon Baptist Convention Health Services, Bamenda, Cameroon
- <sup>c</sup> Center for Women's Reproductive Health, Department of Obstetrics & Gynecology, University of Alabama at Birmingham, Birmingham, AL, United States
- <sup>d</sup> Department of Obstetrics and gynecology, Faculty of Health Sciences, University of Buea, Cameroon
- e School of Nursing and Public Health, University of Kwazulu, South Africa
- f Department of Obstetrics and Gynecology, Yaounde School of Medicine, University of Yaounde, Cameroon
- g Centre Inter-Etats d'Enseignement Supérieur en Santé Publique d'Afrique Centrale, Brazzaville, Congo
- h Department of Gynecologic Oncology and Reproductive Medicine, and Division of Cancer Prevention and Population Sciences, The University of Texas MD Anderson Cancer Center, Houston, TX, United States

#### ARTICLE INFO

#### Keywords: Mobile health Cancer screening Cancer education Cancer prevention Cervical cancer Posttreatment Follow up Telephone reminders Adherence Lost to follow-up Randomized controlled trial Intervention LMICs Cameroon Africa

#### ABSTRACT

Background: Effective management of cervical precancerous lesions requires appropriate posttreatment followup. In Cameroon like in many Low-and-Middle-Income Countries (LMICs), most women treated for cervical precancers do not present for posttreatment follow-up. The aim of this study was to investigate if a telephone reminder sent to women about missed follow-up appointment could reduce the proportion of those who fail to attend the recommended follow-up, and to examine the association of telephone reminders with posttreatment follow-up adherence.

Methods: We carried out a randomized controlled trial nested within a cohort of women screened and treated for cervical precancer (based on positive VIA/VILI results) in a screen-and-treat cervical cancer prevention program in Cameroon. Women who had met clinical criteria for posttreatment follow-up of cervical precancer and did not attend the follow-up appointment within 3 years of precancer treatment were randomly selected and allocated in a 1:1 ratio to the intervention group (receiving a telephone call and text message reminder in addition to the counselling done at the clinic after precancer treatment) and the control group (no telephone reminder after the in-clinic counselling following precancer treatment, per standard of care). Women in the intervention group were contacted by phone, reminded on the importance of posttreatment follow-up they had missed, and invited to return to the clinic for follow-up. The telephone calls were followed by a text message to enhance the understanding of the telephone conversation. The rate of posttreatment follow-up in the intervention group was compared to that of the control group six months after the telephone reminders. A logistic regression analysis was carried out to examine the association between telephone reminders and posttreatment follow-up adherence. Statistical significance was set at p < 0.05.

Results: Between 2022 and 2023, up to 203 women treated for cervical precancers who failed to return to the hospital for posttreatment follow-up within 3 years of receiving precancer treatment were enrolled in this study. Posttreatment follow-up following the telephone reminders was 25.6 % (22/86) and 6.1 % (6/99) in the intervention and control groups, respectively (p < 0.001). In the logistic regression analysis, women who received the telephone reminders were four times [aOR = 3.97, 95 %CI (1.29—12.17), p=0.016)] more likely to return for precancer posttreatment follow-up compared to those who did not receive the telephone reminders. Women treated for low-grade cervical precancerous lesions were over five times [aOR=5.44, 95%CI (1.00 29.63), p = 0.059] more likely to attend posttreatment follow-up compared to those treated for high-grade lesions. HIV status was not associated with adherence to posttreatment follow-up. The overall posttreatment follow-up rate

<sup>\*</sup> Corresponding author at: Department of Obstetrics and gynecology, Yaounde School of Medicine, University of Yaounde, Cameroon. E-mail address: fokom.domgue@gmail.com (J. Fokom Domgue).

increased significantly (p = 0.0024) from 26.45 % (73/276) at baseline, to 36.59 % (101/276) following the intervention.

Conclusion: Telephone reminders of women treated for cervical precancer who missed their posttreatment appointment in screen-and-treat program in Cameroon significantly increased adherence to posttreatment follow-up. Despite these promising findings, the overall rate of missed posttreatment appointment remained high, suggesting that beyond the lack of education, other factors such as cultural, financial and geographic barriers may play a role in the observed poor adherence to posttreatment follow-up in LMICs. Incorporating telephone reminders into the health package of services for cervical precancer prevention in these settings can improve adherence to posttreatment follow-up.

#### 1. Introduction

Posttreatment follow-up among women treated for cervical precancerous lesions in Low-and Middle-Income Countries (LMICs) is generally low compared to High-Income countries (HICs) (Habinshuti et al., 2020; Garcia et al., 2022; Manga et al., 2023). Cervical cancer typically arises from precancerous lesions that appear many years before transformation into invasive malignancy, which allows for screening and treatment of precancerous lesions; ultimately preventing their progression to cervical cancer. Smaller or lower-grade precancerous lesions are usually treated by ablation using cryotherapy or thermal ablation (TA) while larger or higher-grade precancerous lesions are often treated by excision using Large Loop Excision of the Transformation Zone (LLETZ) (World Health Organization, 2021). Continuum of care is critical for women screened and treated for cervical precancer to monitor and re-treat persistent or recurrent lesions as needed. In LMICs where access to basic healthcare services is limited, the World Health Organization (WHO) routinely recommends the first posttreatment follow-up appointment at one year, with a schedule for subsequent follow-ups based on the findings of the first follow-up visit (World Health Organization, 2021). Adherence to posttreatment follow-up should be prioritized for human immunodeficiency virus (HIV)-positive women because they have higher risk of treatment failure. HIV-positive women with CD4 counts fewer than 200 cell/m<sup>2</sup> are more likely to experience recurrence or persistence of precancerous lesions compared to their HIV negative counterparts (World Health Organization, 2021; WHO, 2020; Oga et al., 2016; WHO, 2021). At a time when the WHO is strategizing on eliminating cervical cancer worldwide, posttreatment follow-up should be given utmost importance to ensure that patients treated for cervical precancer do not get lost with persistent or recurrent lesions. In a context where management of invasive cervical cancer is resource-demanding and logistically challenging for both patients and healthcare providers (Ngalla et al., 2024), priority should be given to primary prevention with HPV vaccination (Fokom-Defo et al., 2024) and secondary prevention with screening followed by treatment of precancerous lesions (Fokom-Domgue et al.,

The Cameroon Baptist Convention Health Services (CBCHS), a faithbased healthcare organization operates the largest and most comprehensive cervical cancer prevention program in Cameroon known as the Women's Health Program (WHP). The WHP has adopted the screen-andtreat approach recommended by the WHO for LMICs (WHO, 2021), in which screening is linked to treatment of precancerous lesions to reduce the lost to follow up. From 2007 to 2022 CBCHS-WHP has screened over 120,000 women for cervical cancer from across the country and treated over 5,000 of those who tested positive for cervical precancer. Although beginning 2020, WHP commenced the use Human Papillomavirus (HPV) testing as primary screening for women aged 30 years and older following a pilot study that assessed the feasibility of such approach in this limited-resource setting (Fokom Domgue et al., 2020), the program has relied principally on Visual Inspection with Acetic acid and Lugol's Iodine (VIA/VILI) enhanced by Digital Cervicography (DC). The program has a coordination office and runs a database for women enrolled in cervical cancer screening.

An interobserver agreement of DC interpretations of VIA has

demonstrated that the program is meeting the expected standards in terms of reproducibility and quality assurance (Manga et al., 2015; Lince-Deroche et al., 2018; Susan et al., 2017). WHP adheres to WHO guidelines for posttreatment follow-up of women treated for cervical precancers (DeGregorio et al., 2016, 2017; Johnson et al., 2018; WHO, 2021). In a previous cohort of women screened by the WHP using VIA/ VILI enhanced by DC, women diagnosed with cervical precancer were followed up for five years. Of the 344 women treated for positive VIA/ VILI results in that cohort, only half (190, 55.23 %) returned for posttreatment follow-up within five years following initial precancer treatment (Manga et al., 2023). These findings suggested important lapses in posttreatment follow up among women treated for cervical precancer in Cameroon. In a qualitative study conducted among WHP patients and healthcare providers, three major barriers to posttreatment follow-up emerged: personal barriers (fear, low level of education, and poverty), clinic barriers (healthcare providers' attitudes, cost of services, and inadequate counselling), and social barriers (male partner's influence, distance, and availability of alternative treatment). Among the proposed strategies that loomed from this qualitative study to address the observed barriers to posttreatment follow-up was the use of telephone reminders which laid the foundation of the present study (Manga et al.,

The purpose of this study was to assess the impact of telephone reminders on posttreatment follow-up among women treated for cervical precancers in Cameroon, and to examine the sociodemographic and clinical factors associated with posttreatment follow-up in a cohort of women enrolled in a screen-and-treat cervical cancer prevention program who missed their initial posttreatment appointment.

# 2. Methods

## 2.1. Study design

We carried out a randomized controlled trial nested within a cohort of women treated for cervical precancer in Cameroon. Our study population consisted of women screened and treated for VIA/VILI positive lesions between 2019 and 2020 by the CBCHS-WHP, who did not return for posttreatment follow-up within three years of initial treatment. The study flow-chart is summarized in Fig. 1.This trial has been registered in the Pan African Clinical Trial Registry (pactr.samrc.ac.za) database under the unique identification number: PACTR202503518406969.

#### 2.2. Randomization

Study participants were randomly allocated in a 1:1 ratio into two groups: the intervention and the control groups. A simple ballot procedure was done to determine the start point for allocating enrolled women into the two groups. One was picked as the start point for allocating participants into the intervention group and thus every woman having an odd serial number was allocated to the intervention group, while every woman with an even serial number was allocated to the control group. Given the nature of intervention (telephone reminder), women enrolled in this trial were not concealed to the group allocation. While the WHP data manager who assigned participants to the trial was

not blinded to the group allocation, WHP providers who saw patients in the WHP clinics for posttreatment follow-up were blinded.

#### 2.3. Intervention

Women in the intervention group were contacted by phone, reminded/educated on the importance of posttreatment follow-up, and invited to return to the clinic for a follow-up appointment. Telephone reminders were sent in two steps: In the first step, a phone call was made to the telephone number provided by women in their medical record to ensure that we were dealing with the actual patients. If the women did not respond to the phone call or if the telephone number found in their medical records was unavailable, we repeated the phone call at 5-day intervals up to three times until we were able to talk to the patients. If we failed to communicate with a patient by phone after the third attempt, she was considered unavailable. In the second step, women were sent a text message one week after the phone call. Only women who were successfully contacted by phone call and identified as actual patients were sent the text message.

The text message was sent in English or French to ensure clarity of the messaging and a better understanding of the importance of follow-up. The telephone call and the text message stated that posttreatment follow-up date had passed and why there was a need for women to return to the clinic for follow-up. WHP clinics that could provide the follow-up care based on proximity were indicated to the patients. All phone reminders were made by the WHP data manager to ensure confidentiality and consistency. Adherence to follow-up among women treated for cervical precancer who did not present for posttreatment follow up within 3 years of precancer treatment was measured at 6 months following the phone calls.

We expected that telephone reminders to women who missed their initial posttreatment follow-up appointment would increase adherence to follow-up by at least 10 %. Because we prioritized evaluating the effect of phone reminders on posttreatment follow-up adherence, we opted for the per-protocol approach as the main analysis in this clinical trial. As a result, those who could not be reached by phone were excluded from our primary analyzes.

#### 2.4. Data extraction

Data were abstracted from electronic and paper medical records in collaboration with the WHP data manager, checked for accuracy, coded, and de-identified. Most data were collected at enrollement of study participants. Six months following the telephone calls, adherence to posttreatment follow-up in the intervention and the control groups were compared (Fig. 1).

The study received ethical approval from the CBCHS Institutional Review Board and the Institutional Review Board of the Faculty of Health Sciences of the University of Buea, in Cameroon.

#### 2.5. Measures

Outcome variable:

Our dependent variable was adherence to posttreatment follow-up coded as Yes or No. Posttreatment follow-up adherence (Yes) referred to women treated for VIA/VILI positive lesions in 2019/2020 who had returned to a WHP clinic for posttreatment follow-up visit within three years of initial treatment, i.e, between July 2022 and January 2023. Posttreatment follow-up nonadherence (No) referred to women treated for VIA/VILI positive lesions in 2019/2020 who had not returned for posttreatment follow-up visit within three years of initial treatment, i.e, between July 2022 and January 2023.

#### Co-variates:

For this study, the independent variables were selected based on their potential association with adherence to posttreatment follow-up according to the literature. They were classified into sociodemographic, health-related/clinical and study/environmental characteristics. The sociodemographic variables were: age at the time of precancer treatment ( $<30, 30-49, and \ge 50$  years); level of education [0 to 7 years (primary level), 8 to 14 years (secondary level) and  $\ge 15$  years (tertiary level)]; marital status (single/divorced/widowed; married/living with a partner); employment status (employed; or self-employed). The health-related/clinical variables were: VIA/VILI lesion characteristics (low-grade versus high-grade), HIV status (negative versus positive), and treatment modality (ablation versus excision). The study/environmental variables were: year of precancer treatment (2019 or 2020), study group

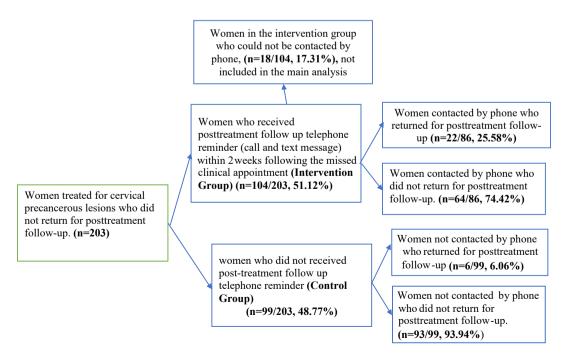


Fig. 1. Study Design, and adherence to Posttreatment Follow-up among Women who received cervical precancer treatment and who missed their initial post-treatment appointment, per protocol analysis. Source: Study Research Team, 2022.

(intervention or control), and region of the country where precancer treatment was provided (Centre, Littoral, Northwest, South, Southwest, and West). Data on selected co-variates were extracted from the CBCHS-WHP database. These data were collected by the WHP data manager from medical records of women screened for cervical cancer in the various WHP sites before the intervention to identify the study population (women who did not attend the posttreatment follow-up), and six months after the telephone reminders to evaluate adherence to post-treatment follow-up following the intervention.

## 2.6. Statistical analysis

#### Clinical trial analysis:

The proportion of women treated for cervical precancer, who missed their initial posttreatment follow-up appointment and who returned to the clinic for posttreatment follow-up within six-month of receiving telephone reminders was compared between the intervention and control groups. While the intention-to-treat (ITT) approach is commonly used for analyzing randomized controlled trials (Detry and Lewis, 2014), priority was given to accurately evaluate the effect of our intervention (telephone reminders) on women's adherence to posttreatment followup. Therefore, the per-protocol (PP) approach in which only participants who adhered to the study protocol are considered, was used as our main analysis (Hernán and Robins, 2017). Since the sociodemographic, clinical and environmental characteristics of women assigned to the intervention group who could not be contacted by phone did not significantly differ from those who could be contacted by phone (data not shown), using the PP approach as our primary analytic method did not eliminate the benefits of randomization. To further mitigate the risk of systematic bias and evaluate the robustness of our findings, we repeated the analyzes using the ITT approach. Because the results of the ITT analysis did not meaninglfully differ from our main findings, they are not presented here.

#### Logistic regression analysis:

In addition to our primary study outcome, the association between telephone reminders and adherence to posttreatment follow-up was examined using a simple logistic regression analysis, while adjusting for potential confounders. All variables with p < 0.2 in the bivariate analysis were entered in the multivariable logistic regression model. A backward stepwise selection was performed, using p-value > 0.2 as removal criterion. In the logistic regression analysis, posttreatment follow-up adherence (Yes/No) was the dependent variable; telephone

reminder (Yes/No) the primary predictor; while other co-variates were the independent variables.

The results of the logistic regression analysis were summarized using odds ratios (ORs) with 95 % confidence intervals (95 % CI) and p-values. Statistical significance was two-sided and set at p < 0.05. All statistical analyses were performed using STATA version 17.

#### 3. Results

#### 3.1. Description of the study population and study arms

A total of 203 women treated for cervical precancer between 2019 and 2020 in the CBCHS-WHP's screen-and-treat program, who did not return for posttreatment follow-up within three years of initial precancer treatment were enrolled in this study (Fig. 1). Eighteen (18) of the 104 women assigned to the intervention group could not be reached by telephone, thus our analysis included 86 (46.49 %) women in this group. All the 99 (53.51 %) women assigned to the control group were included in the study. Most study participants [77.3 % (143/185)] received precancer treatment in 2019. (Table 1).

#### 3.1.1. Sociodemographic characteristics of study participants

Women enrolled in this study were treated in six (Centre, Littoral, Northwest, South, Southwest and West) of the 10 regions of Cameroon, with Littoral being the modal [31.89 % (59/185)] region. The average age of participants was 34.43 years (SD: 09.04 and range: 23-70) and the modal age group was 30 - 49 years [60.54 % (112/185)] (Table 1). Study participants attended some primary school and 40.23 % (70/174) of them completed primary school. Most women [82.7 % (153/185)] enrolled in this trial were self-employed, and involved in small businesses (hairdressing, petit-trading, and farming). More than half [59.02 % (108/185)] were married or living with a partner (Table 1). Consistent with our previous observations, the baseline posttreatment followup rate in this cohort of women treated for positive VIA/VILI results was 26.45 % (73/276), per current CBCHS-WHP's guidelines that recommend counselling about posttreatment follow-up to be done at the clinic with the date of follow-up appointment scheduled by the WHP provider after treatment for cervical precancer and before the patient is discharged.

# 3.1.2. Clinical characteristics of study participants

Up to 23.73 % (42/177) of study participants were living with HIV

Table 1 Sociodemographic Characteristics of Study Participants Source: Study Research Team, 2022.

Variable	Category	Total		Control Group		Intervention Group		p-
		Frequency (n)	Percent (%)	Frequency (n)	Percent (%)	Frequency (n)	Percent (%)	value
Year of precancer treatment	2019	143	77.3	88	88.89	55	63.95	< 0.001
	2020	42	22.7	11	11.11	31	36.05	
Study Region	Centre	34	18.38	21	21.21	13	15.12	0.689
	Littoral	59	31.89	31	31.31	28	32.56	
	Northwest	53	28.65	27	27.27	26	30.23	
	South	17	9.19	8	8.08	9	10.47	
	Southwest	17	9.19	8	8.08	9	10.47	
	West	5	2.7	4	4.04	1	1.16	
Age at precancer treatment	1929	62	33.51	35	35.35	27	31.40	0.099
(Years)	3049	112	60.54	55	55.56	57	66.28	
	>= 50	11	5.95	9	9.09	2	2.33	
<b>Education Level</b>	Primary	70	40.23	32	34.78	38	46.34	0.249
	Secondary	39	22.41	21	22.83	18	21.95	
	Tertiary	65	37.36	39	42.39	26	31.71	
Employment Status	Employed	32	17.3	15	15.15	17	19.77	0,408
	Self-employed	153	82.7	84	84.85	69	80.23	
Marital Status	Married/living with a partner	108	59.02	57	58.16	51	60.00	0.801
	Single/separated/ widowed	75	40.98	41	41.84	34	40.00	

and 81.25 % (143/176) of cervical precancers diagnosed were characterized as low-grade per VIA/VILI examination. Most women with low-grade cervical precancerous lesions received ablative treatment [(81.22 % (147/181)], per standard of care (Table 2). During the study period, 15.14 % (28/185) of treated women who did not present for the post-treatment follow within 3 years of receiving precancer treatment, returned to the WHP for follow-up appointment. Of these 28 women who returned for posttreatment follow-up 6 months after the telephone reminders, 22 (78.57 %) were in the intervention group and 6 (21.43 %) in the control group (Table 2). There was no statistically significant difference between the intervention and control groups, in terms of sociodemographic, clinical and environmental characteristics, except for year of precancer treatment. (Tables 1 and 2).

# 3.2. Adherence to posttreatment follow-up among women treated for cervical precancer who missed their initial clinical appointment, overall and by study arm

Of the 276 women treated for cervical precancer in 2019/2020, 203 (73.55 %) did not return to the hospital for posttreatment follow-up within 3 years of receiving precancer treatment. These 203 women were randomly assigned into intervention [104 (51.23 %)] and control [99 (48.77 %)] groups.

Six months after the telephone reminders, 25.59 % (22/86) of women in the intervention arm presented to a WHP clinic for post-treatment follow-up versus only 6.06 % (6/99) of women in the control arm. The average posttreatment follow-up rate among women enrolled in this clinical trial during the study period (i.e., six months after the telephone reminders) was 15.14 % (28/185). The overall posttreatment follow-up (including all women treated for cervical precancer in 2019/2020) increased significantly from 26.45 % (73/276) before the intervention (at baseline), to 36.59 % [(101/276), p = 0.0024] following the intervention. The 10.14 % increase in the cervical precancer posttreatment follow-up adherence achieved between the baseline and the post-intervention evaluation was mainly attributed to the telephone reminders as 22 of the 28 women who returned to the clinic for post-treatment follow-up were coming from the intervention group (Fig. 2).

# 3.3. Impact of telephone reminders and factors associated with adherence to posttreatment follow-up among women treated for cervical precancer

In the per-protocol analysis, of the 28 women who presented for posttreatment follow-up during the study period, 22 (25.58 %) were in the intervention group and 6 (6.06 %) in the control group (p < 0.001) (Fig. 1 and Fig. 2). There was a statistically significant association between cervical precancer posttreatment follow-up adherence and telephone reminders when the intervention group was compared to the control group.

In the logistic regression analysis, women who received the telephone reminders were four times [adjusted odds ratio (aOR) = 3.97, 95 % CI (1.29–12.17), p = 0.016)] more likely to return to the hospital for posttreatment follow-up compared to those who did not receive telephone reminders. (Fig. 2 and Table 3).

Year of precancer treatment was found to be significantly associated

with adherence to posttreatment follow-up, with women who received treatment in 2020 being nearly 7 times [aOR  $=6.87,\,95$  % CI (2.32–20.40), p =0.001] more likely to attend posttreatment follow-up compared to those who were treated in 2019. (Fig. 2 and Table 3).

Women treated for low-grade cervical precancerous lesions were over five times [aOR = 5.44, 95 % CI (1.00–29.63), p=0.059] more likely to attend posttreatment follow-up compared to those treated for high-grade lesions. No statistically significant association was found between HIV status and posttreatment follow-up (Fig. 2 and Table 3).

#### 4. Discussion

In this pilot clinical trial, we assessed the impact of a simple and lowcost intervention (telephone reminders) on adherence to posttreatment follow-up among women treated for positive VIA/VILI screening results who failed to attend their scheduled follow-up appointment, within a screen-and-treat cervical cancer prevention program in Cameroon. Our study demonstrated that telephone reminders improved follow-up adherence among women treated for cervical precancer who had missed posttreatment follow-up appointments. This finding is consistent with previous reports on the efficacy of mobile technologies from other LMICs. In a study evaluating follow-up for cervical cancer screening among women with positive HPV test in Honduras, a single phone call was effective to prompt those who received ablative treatment for cervical precancer to return for rescreening (Thomson et al., 2020). In another study to improve routine childhood immunization using telephone reminders in Nigeria, women in the intervention arm reported higher uptake of childhood immunization compared to their counterparts in the control arm (Brown and Oluwatosin, 2017). A third study in India found that participation in a telephone call intervention can improve hypertensive patients' compliance and retention in care (Kannure et al., 2021).

In our study, the cost of the intervention we implemented (telephone reminder) in terms of personnel time/level of effort and telephone bill could be estimated between one to three USDs per patient, and we had to call 86 women to have 22 (25.58 %) of them return for posttreatment follow-up within six months of receiving the telephone reminders. A few USDs call per patient to remind women about the importance of posttreatment follow-up appears to be affordable, feasible and acceptable in most LMICs. In many HICs like Australia, telephone reminder is part of the basic health package, including for preventive services (Beauchamp et al., 2020). Though the availability and use of mobile phones is on the rise in most LMICs, there are still some low-income groups who cannot afford mobile phones. Even when the mobile phones are available, cellular network in many remote areas in LMICs remains inadequate. This can create a technological barrier to introducing the telephone reminder model into the healthcare package in some parts of LMICs.

The year when precancer treatment was provided was significantly associated with posttreatment follow-up in our study. Women who were reminded to come for posttreatment follow-up at fewer than three years were more likely to attend their clinical appointment compared to those who were reminded later . This could be an indication that telephone reminders work better for shorter appointments than for longer ones. In another study of women screened for cervical cancer in Cameroon, a

 Table 2

 Clinical characteristics of study participants Source: Study Research Team, 2022.

Variable	Category	Total		Control Group		Intervention Group		p-value
		Frequency (n)	Percent (%)	Frequency (n)	Percent (%)	Frequency (n)	Percent (%)	
HIV status	Positive	42	23.73	25	26.60	17	20.48	0.34
	Negative	135	76.27	69	73.40	66	79.52	
Lesion characteristics	Low-Grade	143	81.25	78	82.98	65	79.27	0.529
	High-Grade	33	18.75	16	17.02	17	20.73	
Treatment modality	Ablative	147	81.22	80	84.21	67	77.91	0.278
	Excisional	34	18.78	15	15.79	19	22.09	

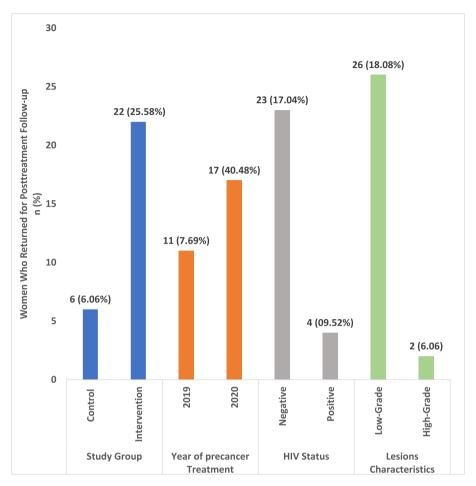


Fig. 2. Proportion of women treated for cervical precancer in Cameroon who presented to the hospital for posttreatment follow-up after the intervention per Study Group, Year of precancer treatment, HIV status and precancerous lesions characteristics.

follow-up rate of 99.1 % after one month of receiving ablative treatment for precancerous lesions was reported (Viviano et al., 2017). In additon to the closer follow-up appointment date, the high rate of follow-up observed in this study by Viviano et al, was explained by the fact that treated women who returned to the hopsital for follow-up were reimbursed transportation fees, unlike in our study where women did not receive any financial incentive for returning to the clinic for follow-up. In the WHP's cervical cancer prevention program, women are usually given a follow-up appoitment one year after receiving treatment for precancer, unless they develop serious side effects or have symptoms that prompt them to return to the clinic ealier. As noted in the qualitative study by Manga et al., forgetfulness was a major reason for low posttreatment follow-up in our setting (Manga et al., 2019). In the absence of complications or concerns related to their care, it is common for patients to forget longer appointments compared to shorter ones. Since posttreatment follow-up appointment for cervical precancer are usually given after a year within the WHP, the risk of appointment forgetfulness should not be minimized, especially in the absence of any reminder. Thus, it is important to explore simple and easy-to-implement strategies like telephone reminders to mitigate this forgetfulness.

Women treated for high-grade precancerous lesions were less likely to adhere to posttreatment follow-up compared to those treated for low-grade precancerous lesions. These findings are not corroborated by a previous study conducted in Honduras, in which women with high-grade precancerous lesions had a higher rate of posttreatment follow-up one year after treatment (Slavkovsky et al., 2020). This discrepancy could be explained to some extent by the cultural and socio-demographic differences between the two populations one one hand,

and by the definition of posttreatment follow-up adherence on the other hand, which was determined within three years of initial treatment in our trial, compared to the study by Slavkovsky, *et al.*, where posttreatment follow-up adherence was defined at one year after receiving precancer treatment. People with high-grade lesions are more likely to have personal barriers like fear of being diagnosed with a persistent or progressing disease (Manga et al., 2019). Therefore, the lower odds of posttreatment follow-up observed among women with high-grade lesions in our study could be caused, at least in part, by the greater apprehension or fear of recurrent disease, compared to women treated for low-grade lesions. Furthermore, because women with high-grade cervical lesions are more likely to have a lower health literacy level compared to those diagnosed with lower-grade cervical lesions, they may be less aware of the need for posttreatment follow-up compared to the later.

There was no significant association between HIV status and adherence to posttreatment follow-up. In a cross-sectional study based on a secondary analysis of the 2018 demographic and health survey in Cameroon, HIV positive women were more likely to seek cervical cancer prevention services than HIV negative women (Okyere et al., 2021). Consistent with our findings, a previous report from a cohort of women screened and treated within the WHP found no association between HIV status and adherence to posttreatment follow-up after 5 years of receiving treatment for cervical precancerous lesions (Manga et al., 2023). Since the risk of disease recurrence and treatment failure is higher among HIV positive women compared to HIV negative women (De Vuyst et al., 2014), initiatives to improve adherence to posttreatment follow-up in high-burden settings should focus on high-risk groups

**Table 3**Factors associated with adherence to Posttreatment follow-up among women treated for cervical precancer in Cameroon who missed their scheduled clinical follow-up appointment. Source: Study Research Team, 2022.

Variable	Posttreatment Follow-up		cOR (95 % CI)	p- value	aOR (95 % CI)	p- value
	No (%)	Yes (%)				
Year of Treatr	nent					
2019	132	11	1			
	(92.31)	(7.69)				
2020	25	17	8.16	< 0.001	6.87	< 0.001
	((59.52)	(40.48)	(3.4		(2.35	
Ct 1 C			19.5)		20.45)	
Study Group Control	93	6 (6.06)	1			
Collifor	(93.94)	0 (0.00)	1			
Intervention	64	22	5.33	0.001	3.97	0.016
intervention	(74.42)	(25.58)	(2.1	0.001	(1.3	0.010
	(/ 11 12)	(20.00)	13.9)		12.2)	
Age (Years)			10.5)		12.2)	
23 – 29	50	12	1			
	(80.65)	(19.35)				
30 – 49	97	15	0.64	0.301		
	(86.61)	(13.39)	(0.3			
			1.5)			
>= 50	10	1 (9.09)	0.42	0.425		
	(90.91)		(0.1			
			3.6)			
<b>Education Lev</b>	/el					
Primary	59	11	1			
	(84.29)	(15.71)				
Secondary	30	9	1.61	0.344		
	(76.92)	(23.08)	(0.6			
		_	4.3)			
Tertiary	58	7	0.65	0.401		
	(89.23)	(11.11)	(0.2			
0			1.8)			
Occupation Self-	130	22	1			
employed	(85.62)	(14.38)	1			
Employed	26	7	0.73	0.532		
Linployed	(81.25)	(10.77)	(0.3	0.002		
	(01.20)	(10177)	2.0)			
Marital Status	3					
Married	93	15	1			
	(86.11)	(13.89)				
Single	62	13	1.3	0.525		
	(82.67)	(17.33)	(0.6			
			2.9)			
HIV Status						
Negative	112	23	1			
	(82.96)	(17.04)				
Positive	38	4 (9.52)	1.95	0.244		
	(90.48)		(0.6			
Complete 1 To 1	Cha		6.0)			
Cervical Lesio High-Grade	on Character 31		1			
rugu-Grade	(93.94)	2 (6.06)	1			
Low-Grade	(93.94)	26	3.44	0.104	5.44	0.049
TOM-GIAGE	(81.82)	(18.18)	(0.8	0.104	(1.0	0.043
	(01.02)	(10.10)	15.3)		29.6)	
			10.0)		27.07	
Treatment Mo	oanty					
Treatment Mo	123	24	1			
	123		1			
	-	24 (16.33) 4	0.68	0.509		
Ablative	123 (83.67)	(16.33)		0.509		

cOR: crude odds ratio; aOR: adjusted odds ratio; 95%CI: 95% confidence interval.

such as HIV positive women.

Our study had some limitations. Although most women enrolled in this trial provided contact information in their medical records, nearly one-fifth of those assigned to the intervention arm who had reported a phone number through which they could be contacted, were

unreachable during the study period. Despite the progress made to improve access to digital technology in Africa over the past decades, our finding reflects the relatively low penetration of mobile phone technology in LMICs especially in rural and remote areas; and underscores the need for alternative and culturally appropriate methods such as patient navigation tools adapted to the poor transportation network seen in many LMICs and liaison with community health workers to better link patients in the community with the health system (Fokom Domgue et al., 2020). Due to the lack of relevant data, additional confounders such as the place of women's residence (rural/urban), their socio-economic status (income) and their distance to the closest healthcare facility where they could go for posttreatment follow up were not considered as co-variates. As a result, these common predictors of access to cervical screening and/or posttreatment follow-up in LMICs (Manga et al., 2019; Cunningham et al., 2015) may have contributed to some extent, to yield a certain level of selection bias in our study population. However, the risk of bias associated with these factors was mitigated by the randomization.

While phone calls and text messages in this trial were only sent to women who failed to attend their follow-up appointment (i.e., after the date of the missed clinical appointment), sending telephone reminders to all treated women prior to their scheduled posttreatment date might have further contributed to increase women's adherence to follow-up. In subsequent efforts, we plan to assess the feasibility and cost-effectiveness in our setting of this systematic approach that seems to be more pro-active, compared to the targeted approach used in the present study which was more delayed.

#### 5. Conclusion

In LMICs like Cameroon, telephone reminders have the potential to increase posttreatment follow-up adherence among women treated for cervical precancer who do not present to the hospital for follow-up services. Incorporating this simple and affordable intervention into cervical cancer prevention programs in high-burden settings could improve screening uptake and posttreatment follow-up, thereby contributing to the reduction of the burden of cervical cancer. For a better outcome, telephone reminders should be done earlier, i.e, a few weeks before the posttreatment appointment date, and directed towards high-risk groups such as HIV positive women and those with a low level of education. Health seeking behavior and women's awareness and knowledge about cervical cancer should be equally enhanced by healthcare providers and other community stakeholders to improve adherence to posttreatment follow-up. Further studies involving larger sample sizes and accounting for additional predictors such as socioeconomic status of women, their place of residence, and the distance to the healthcare facility are needed to further assess the costeffectiveness of a strategy based on telephone reminders in improving cervical precancer posttreatment follow-up in LMICs.

# Funding/Support

None.

#### CRediT authorship contribution statement

Joseph F. Nkfusai: Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Data curation, Conceptualization. Simon M. Manga: Writing – review & editing, Validation, Project administration, Investigation. Kathleen Nulah: Software, Investigation, Formal analysis, Data curation. Calvin Ngalla: Writing – review & editing, Investigation. Claude Ngwayu: Writing – review & editing, Investigation. Charlotte B. Mbuwir: Writing – review & editing, Investigation. Nicholas Tendongfor: Writing – review & editing, Supervision. Edie Gregory Halle Ekane: Writing – review & editing, Supervision. Joël Fokom Domgue: Writing – review & editing,

Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

## **Ethics approval**

Ethical approval for the study was sought from the Ethics Committee of the Faculty of Health Sciences, University of Buea and the Ethics Committee for Human Health Research of the CBCHS, Cameroon.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### Acknowledgements

The authors are grateful to all who took part in this study.

#### References

- Habinshuti, P., Hagenimana, M., Nguyen, C., Park, P.H., Mpunga, T., Shulman, L.N., et al., 2020. Factors associated with loss to follow-up among cervical cancer patients in rwanda. Ann Glob Heal. 86 (1), 1–13.
- Garcia, A., Juarez, M., Sacuj, N., Tzurec, E., Larson, K., Miller, A., et al., 2022. Loss to follow-up and the care cascade for cervical cancer care in rural guatemala: a crosssectional study. JCO Glob Oncol. 8, 1–9.
- Manga, S.M., Nkfusai, J.F., Nulah, K.L., Manjuh, F., Fokom-domgue, J., Ye, Y., (2023) Gynecologic Oncology Reports Factors associated with adherence to post-treatment follow-up among a cohort of women with acetic acid / Lugol 's iodine positive lesions of the cervix in Cameroon: A retrospective cohort study. Gynecol Oncol Reports [Internet]. 49(August):101269. Available from: https://doi.org/10.1016/j. gore.2023.101269.
- World Health Organization, (2021). Web Annex A. Syntheses of evidence [Internet].
  WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention. Available from: https://apps.who.int/iris/bitstream/handle/10665/342366/9789240030886-ene.pdf.
- WHO, (2020). Global strategy to accelerate the elimination of cervical cancer as a public health problem and its associated goals and targets for the period 2020 2030. Vol. 2, United Nations General Assembly. 1–3.
- Oga, E.A., Brown, J.P., Brown, C., Dareng, E., Adekanmbi, V., Odutola, M., et al., (2016). Recurrence of cervical intraepithelial lesions after thermo-coagulation in HIV-positive and HIV-negative Nigerian women. BMC Womens Health [Internet]. 16(1) 1–8. Available from: https://doi.org/10.1186/s12905-016-0304-8.
- WHO, (2021). National Guideline Clearinghouse | WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention. [Internet]. Second Edi. Geneva: World Health Organization. Available from: http://www.guideline.gov/content.aspx?f=rss&id=49521&osrc=12.
- Ngalla, C., Didymus, J., Manjuh, F., Nwufor, M., Nkfusai, J., Elit, L., Fokom Domgue, J., Challenges faced in managing cervical cancer patients who present post-operatively with more advanced disease in LMICs: Case studies from Cameroon. Gynecol Oncol Rep. 2024 Aug 13;55:101485. doi: 10.1016/j.gore.2024.101485. PMID: 39247488; PMCID: PMC11378922.
- Fokom Domgue J, Futuh B, Ngalla C, Kakute P, Manjuh F, Manga S, Nulah K, Welty E, Schmeler K, Welty T. Feasibility of a community-based cervical cancer screening with "test and treat" strategy using self-sample for an HPV test: Experience from rural Cameroon, Africa. Int J Cancer. 2020 Jul 1;14(1):128-138. doi: 10.1002/ijc.3246. Epub 2019 Nov 9. PMID: 31633801.
- DeGregorio, G.A., Bradford, L.S., Manga, S., Tih, P.M., Wamai, R., Ogembo, R., et al., 2016. Prevalence, predictors, and same day treatment of positive VIA enhanced by

- digital cervicography and histopathology results in a cervical cancer prevention program in Cameroon. PLoS One 11 (6).
- Manga, S., Parham, G., Benjamin, N., Nulah, K., Sheldon, L.K., Welty, E., et al., 2015. Cervical cancer screening in cameroon: interobserver agreement on the interpretation of digital cervicography results. J Low Genit Tract Dis. 19 (4), 288–294.
- DeGregorio, G., Manga, S., Kiyang, E., Manjuh, F., Bradford, L., Cholli, P., et al., 2017. Implementing a fee-for-service cervical cancer screening and treatment program in cameroon: challenges and opportunities. Oncologist. 22 (7), 850–859.
- Johnson, L.G., Armstrong, A., Joyce, C.M., Teitelman, A.M., Buttenheim, A.M., 2018. Implementation strategies to improve cervical cancer prevention in sub-Saharan Africa: a systematic review. Implement Sci. 13 (1), 1–18.
- Lince-Deroche N, Van Rensburg C, Roseleur J, Sanusi B, Phiri J, Michelow P, et al. Correction: Costs and cost-effectiveness of LEEP versus cryotherapy for treating cervical dysplasia among HIV-positive women in Johannesburg, South Africa (PLoS ONE (2018) 13:10 (e0203921) DOI: 10.1371/Journal.Pone.0203921). PLoS One. 2019:14(2):1–13.
- Susan, C.U., Orang'o, E.O., Liu, T., Christoffersen-Deb, A., Itsura, P., Oguda, J., et al., 2017. Use of visual inspection with acetic acid, Pap smear, or high-risk human papillomavirus testing in women living with HIV/AIDS for posttreatment cervical cancer screening: Same tests, different priorities. AIDS 31 (2), 233–240.
- Manga, S., Kiyang, E., DeMarco, R.F., 2019. Barriers and facilitators of follow-up among women with precancerous lesions of the cervix in Cameroon: a qualitative pilot study. Int J Womens Health. 11, 229–239.
- Detry, M.A., Lewis, R.J., 2014. The intention-to-treat principle: how to assess the true effect of choosing a medical treatment. JAMA 312 (1), 85–86. https://doi.org/10.1001/jama.2014.752314c.
- Hernán, M.A., Robins, J.M., 2017. Per-protocol analyses of pragmatic trials. N Engl J Med. 377 (14), 1391–1398. https://doi.org/10.1056/NEJMsm1605385.
- Thomson, K.A., Sandoval, M., Bain, C., Holme, F., Bansil, P., Figueroa, J., et al., 2020.

  Recall efforts successfully increase follow-up for cervical cancer screening among women with human papillomavirus in Honduras. Glob Heal Sci Pract. 8 (2), 290–299.
- Brown, V.B., Oluwatosin, O.A., 2017. Feasibility of implementing a cellphone-based reminder/recall strategy to improve childhood routine immunization in a low-resource setting: a descriptive report. BMC Health Serv Res. 17 (Suppl 2).
- Kannure, M., Hegde, A., Khungar-Pathni, A., Sharma, B., Scuteri, A., Neupane, D., et al., 2021. Phone calls for improving blood pressure control among hypertensive patients attending private medical practitioners in India: findings from Mumbai hypertension project. J Clin Hypertens. 23 (4), 730–737.
- Beauchamp, A., Mohebbi, M., Cooper, A., Pridmore, V., Livingston, P., Scanlon, M., et al., 2020. The impact of translated reminder letters and phone calls on mammography screening booking rates: two randomised controlled trials. PLoS One 15 (1), 1–16.
- Viviano, M., Kenfack, B., Catarino, R., Tincho, E., Temogne, L., Benski, A.C., et al., 2017.
  Feasibility of thermocoagulation in a screen-and-treat approach for the treatment of cervical precancerous lesions in sub-Saharan Africa. BMC Womens Health 17 (1), 2.
- Slavkovsky, R.C., Bansil, P., Sandoval, M.A., Figueroa, J., Rodriguez, D.M., Lobo, J.S., et al., 2020. Health outcomes at 1 year after thermal ablation for cervical precancer among human papillomavirus— and visual inspection with acetic acid—positive women in honduras. JCO Glob Oncol. 6, 1565–1573.
- Okyere, J., Duodu, P.A., Aduse-Poku, L., Agbadi, P., Nutor, J.J., 2021. Cervical cancer screening prevalence and its correlates in Cameroon: secondary data analysis of the 2018 demographic and health surveys. BMC Public Health 21 (1), 1–8.
- De Vuyst, H., Mugo, N.R., Franceschi, S., McKenzie, K., Tenet, V., Njoroge, J., Rana, F.S., Sakr, S.R., Snijders, P.J.F., Chung, M.H., Meyers, C., 2014. Residual disease and HPV persistence after cryotherapy for cervical intraepithelial neoplasia grade 2/3 in hivpositive women in Kenya. PLoS One 9 (10). https://doi.org/10.1371/journal.pone.0111037.
- Cunningham, M.S., Skrastins, E., Fitzpatrick, R., et al., 2015. Cervical cancer screening and HPV vaccine acceptability among rural and urban women in Kilimanjaro region, Tanzania. BMJ Open 5. https://doi.org/10.1136/bmjopen-2014-005828.
- Fokom-Defo, V., Dille, I., Fokom-Domgue, J., 2024 Mar. Single dose HPV vaccine in achieving global cervical cancer elimination. Lancet Glob Health. 12 (3), e360–e361. https://doi.org/10.1016/S2214-109X(24)00009-3. PMID: 38365404.
- Fokom-Domgue, J., Vassilakos, P., Petignat, P., 2014 Aug. Is screen-and-treat approach suited for screening and management of precancerous cervical lesions in Sub-Saharan Africa? Prev Med. 65, 138–140. https://doi.org/10.1016/j. ypmed.2014.05.014. Epub 2014 May 28. PMID: 24879892.