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"I'm here to save my life:" a qualitative study of experiences navigating a cryotherapy referral system for human papillomavirus-positive women in western Kenya

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Abstract

Objectives: We sought to understand the beliefs, social norms and logistical factors that affect HPV-positive women's uptake of cryotherapy treatment as part of a two-part cervical cancer screening strategy in rural Kenya.

Design: In-depth interviews within a parent cluster-randomized trial

Setting: Government-run county hospital in western Kenya.

Participants: 273 of 372 (73.4%) HPV-positive women who underwent cryotherapy

Results: Many women feared that an HPV infection meant they would develop cancer. Almost all women reported initial fear of the treatment procedure, followed by a more positive experience than anticipated. Lacking funds for transportation to the treatment site was the most common barrier. Women felt that decentralized treatment would be the most important facilitator of greater access. Spousal encouragement and financial support were key facilitators of treatment access, however many women felt that other husbands in the community would not be supportive. Women described successfully acquiring treatment as empowering, and almost all would recommend seeking cryotherapy to other women who test HPV positive. Most felt eager to share their own experiences with others to encourage treatment.

Conclusions: The main facilitators of treatment access were understanding of the health risks and sense of empowerment. A decentralized treatment model or transportation support may facilitate access, along with improved health messaging about HPV infection, cancer, and the treatment process. Focusing on women's personal feelings of empowerment may further improve uptake and satisfaction. This data will be used to design a strategy to improve linkage to treatment.

Trial Registration: NCT02124252

Strengths and Limitations

- This study provides insight into women’s experience obtaining cryotherapy after a receiving positive HPV test result in western Kenya.
- The perspectives provided will allow for improved contextualization of cervical cancer prevention programs in similar settings.
- These qualitative findings are exploratory, and may not be reflective of larger patterns or associations.
- Women were interviewed by trained study staff, so there may have been social desirability bias.
- We did not interview women who were lost-to-follow-up, and may have therefore have had even more barriers than those identified in this study

Article Summary

- This study used in-depth interviews and qualitative data analysis methods to understand the barriers and facilitators of treatment access among HPV-positive women seeking treatment in rural Kenya.
- Women were recruited for an IDI after undergoing cryotherapy at a county referral hospital.
- Researchers sought wide inclusion of women often underrepresented in research to understand potentially unique experiences with care.

Introduction:

Cervical cancer, despite being one of the most preventable cancers through vaccination and screening, remains the fourth most common cancer among women worldwide.[1] Now rare in wealthier countries due to the success of cytology-based prevention programs, cervical cancer continues to be a major public health issue in low and middle-income countries (LMICs). Effective population-based screening, coupled with linkage to treatment for screen-positive women, is critical to preventing the development of cervical cancer. In Kenya, where screening rates range between 3 and 14%, cervical cancer is the second most common cancer in women, and the leading cause of cancer related mortality.[2]

Strategies to address the lack of screening programs in LMICs include simpler screening techniques coupled with cryotherapy for women who screen positive. Cryotherapy is relatively inexpensive, can be performed by non-physician providers and does not require electricity. It has been promoted along with Visual Inspection with Acetic Acid (VIA) as a part of a same day “see & treat” strategy, although the expense and logistical challenges of maintaining supplies, space, and personnel for cryotherapy in remote settings make single visit strategies impossible in most settings.[3, 4]

Another simple screening technique is low-cost human papillomavirus (HPV) testing.[5, 6] The World Health Organization incorporated the growing body of evidence supporting HPV testing into recommendations for screening programs in low resource settings.[7] The current guidelines include HPV primary screening as the preferred modality, followed by cryotherapy. As HPV testing has become more widely available and the evidence for its use more convincing, programs are starting to move from “see & treat” to “screen & treat,” referring women for treatment based on a positive HPV result. While this may be more effective at decreasing cervical precancer and cancer, there are no currently available HPV tests that allow for same-visit results. Therefore, programs must take into consideration how to deliver HPV test results and counseling in a way that fosters understanding and facilitates women’s uptake of the appropriate follow-up. An effective HPV-based screening program must take into account the multitude of sociocultural factors such as stigma, fear, and misperceptions, along with the logistical and health systems factors that affect a woman's decision-making and ability to seek screening, understand her results and obtain treatment if needed.

While multiple studies have evaluated effective screening methods for women in western Kenya, there remains a gap in understanding effective strategies to link women who screen positive for HPV to appropriate follow-up and treatment.[8-12] Understanding the knowledge, beliefs, social norms, and logistical factors that affect women's decision and ability to seek treatment are essential in the design of effective context- specific treatment strategies. We used the Consolidated Framework for Implementation Research (CFIR) to explore the contextual factors that may have facilitated HPV-positive women's access to appropriate treatment within a community-based screening program. [13]

Materials and Methods:

Study Design

We utilized qualitative data to explore the barriers and facilitators of treatment access for women who tested HPV positive as part of a two-phase cluster randomized trial in rural western Kenya.[14] In the first phase, 12 communities in Migori County were randomized to screening using self-collected HPV tests either through community health campaigns (CHCs) or in health facilities. In both the CHC and health facility arms, women who tested HPV positive were notified of their results and referred to the Migori County Hospital for treatment with cryotherapy. After treatment, women were invited to participant in an in-depth-interview (IDI) regarding their experience.

The distance between Migori County Hospital and the 12 study communities ranged from 11 to 94 kilometers. Transport around the county was available via motorcycles, public buses and private taxis. In the hospital compound, treatment was provided by nurses who had undergone additional training in both cryotherapy and study procedures prior to study initiation. The medical superintendent and an experienced nurse facilitator provided supervision as needed. Women underwent VIA prior to treatment, followed by cryotherapy unless the cervical anatomy was abnormal, the lesion was too large for the probe, or there was suspicion for cancer. In the first two cases, the woman would be referred for LEEP within the same hospital. If there was suspicion for cancer, she was offered a biopsy and referred for management of cancer. All costs associated with cryotherapy or LEEP were covered by the study. Women did not receive compensation for transport or monetary incentives for participation in the study.

Data Sources

IDI guides were developed using selected CFIR constructs to elicit responses about the client-sided experience and perceptions of treatment (Table 1). Selected constructs included adaptability, patient needs and resources and complexity of proposed intervention methods. IDI guides were developed in English and translated and conducted in the most common local languages (Dholuo and Kiswahili) by researchers fluent in those languages. The first part of the IDIs consisted of closed-ended questions about sociodemographic characteristics, sexual behavior, gynecological history, HIV status, cervical cancer screening, and HPV. Interviewers entered this data directly into Open Data Kit installed onto study tablets. The second part of the interviews consisted of open-ended questions that probed women on what they understood about HPV and treatment for HPV, their feelings and experience with treatment, barriers and facilitators to treatment, stigma and desire for privacy, and male and community leader roles in facilitating cervical cancer prevention. This data was recorded on the tablets, and then transcribed and translated. All translations were reviewed with the audio by the study coordinator for accuracy.

Data Analysis

Using grounded thematic analysis, one member of the research team created the codebook using the IDI guide for structure and four sample interviews to identify additional themes. The codebook was then reviewed and revised by the entire team, followed by a round in which all four researchers sample coded ten interviews to test and revise the codebook. All analysis and codebook development was done using NVivo 11™ software (QSR International, London, United Kingdom). The team then met to discuss and make final revisions to the codebook. All interviews were coded twice by two separate members of the research team. Coding reports were then reviewed collaboratively to identify important themes and finalize mapping onto the modified CFIR framework. We used the SRQR checklist when writing our report.[15]

Ethical Considerations

The Kenya Medical Research Institute Scientific and Ethics Review Unit, The Duke University Institutional Review Board and the University of California, San Francisco Human Research Protection Program Institutional Review Board reviewed and approved this study. All participants gave their written informed consent to participate in the study prior to data collection.

Results:

Between February and December 2016, 5898 women underwent cervical cancer screening in both CHC and health facilities and 1043 (17.4%) tested positive for HPV. Out of these women, 399 (38.3%) women presented for treatment at Migori County Hospital and 372 (35.6%) underwent cryotherapy. Three women were referred for LEEP and one for invasive cancer management. Among the 372 treated HPV-positive women, 273 women (73.4%) completed an in-depth interview after their treatment. There was no difference in the clinical or demographic characteristics in the participants from the original study arm, or between those who agreed to an interview and those who declined. Women traveled a mean of 37 kilometers to get to Migori for treatment, and almost all used a paid form of transportation (bus, taxi or motorbike).

Knowledge and perceptions of HPV positivity

Women reported a generally high level of knowledge about the relationship between HPV and cervical cancer, and the role of treatment in protecting their health. Specifically, many understood that the recommended treatment was simpler and more effective than it would be if HPV developed into cervical cancer.

> *“I learnt that, having HPV doesn’t mean you have the disease, it is just a sign that it may develop in to a disease and when you have the virus and it is detected early enough it can be treated”*

Although knowledge statements were common, women expressed fear, anxiety and misperceptions about their positive HPV results and the association with cancer. This was reflected in women’s feelings around the time they received their results and their concern that the treatment would not “cure” their cancer.

> *“I felt pain at heart, since I do hear that those with cancer do not survive, even now I still have no assurance of good health.”*

Though some women reported worry or anxiety about their test result, many felt relief that they were now aware of their HPV status and could get treatment.

> *“What came into my mind after I was confirmed HPV positive was just on how I can access treatment my focus now is how I can be on treatment and that is my key challenge as at now.”*

Many women were concerned about the futility of treatment in situations where they perceived little control over possible reinfection. Concerns were raised about safe relations with their husband, inability to negotiate condoms and concerns about [re]infection among co-wives.

> *"It is said that men are the one who infects us, and us still being a young couple we are bound to have sexual relations, what can be done so to men so that they do not spread the disease?"*

> *"Supposing I have a co-wife, how will I know that she has also been treated so that we can all be free and not use condoms?"*

Treatment Experience

Women were almost uniformly positive about provider respect, privacy, adequate explanation, and ability to ask and have their questions answered. Most women also reported minimal pain or cramping, with no reported complications with the procedure. Overall, women expressed relief that the procedure was not as difficult as they had feared, with responses similar to the comment below.

> *"When I came from home, people were saying that this treatment is painful but I have not felt any pain. I have found it to be good and the pain that people are talking about is not there."*

When asked how to improve the treatment experience, women had limited suggestions, or focused on access issues. This may not reflect satisfaction with the treatment model as much as a feeling that it was the role of "health care providers or "doctors" to "improve the experience". *"It is you as healthcare providers to find on ways of making it more comfortable."*

Despite reporting adequate explanation and overall treatment satisfaction, a number of unanswered questions or misperceptions regarding cervical cancer or follow-up arose throughout the interviews. Unanswered questions revealed underlying fears about extent of disease/outcomes of treatment (future fertility, death from cancer, etc). Many women were under the impression that they would be given drugs to treat HPV, like treatment for malaria or HIV management. *"I have learnt that in case I will be given drugs then I will have to take them to help prevent the virus from advancing into cervical* *cancer."* Women who mentioned drugs recounted that they were *told* they would be given drugs, although this was not an intended part of the health messaging during screening or treatment.

Some women believed that if they were infected with HPV, they would not be able to give birth, or they should not get pregnant because the fetus would be infected with HPV. Related to the fear of infertility, women reported believing that family planning methods caused their positive HPV result or would cause cervical cancer.*"I thought that I had cervical cancer because since I went for family planning [IUCD]. I have not been feeling okay in the uterus."*

Identifying Specific Barriers and Facilitators to Treatment Access

When women were asked whether they encountered any barriers or difficulty accessing treatment, and most answered no. However, when prompted, many confirmed that they had to miss work, struggled to find childcare or transportation funds, or traveled a long distance. Some women expressed the belief that if a woman is sick or valued her health, there were no barriers that could stop her from accessing treatment in statements like the following: *"It can only be far for someone who is not sick but if you are sick, you cannot say that it is far. I'm here to save my life."*

Lack of access to means of transportation and/or funds to hire transport were the main barriers that resulted in delays in treatment. Women also worried about future transport costs if the disease progressed, explicitly stating that they anticipated missing future appointments.

> *"I do not know what to tell you. If you have money you can access everywhere, but if you do not you cannot make it on foot. The poor will die of even diseases that can be treated unlike the rich."*

When asked about how to make treatment access easier, many women mentioned that telling their own story of treatment to women who tested positive for HPV would be helpful, suggesting that peer education and social support may play a large role in decision to get treated. Women wanted to publicize that treatment was free, easy, quick and important for women's long-term health.

> *"When the [positive] results came I was surprised. I then took time and went to my friends who also were HPV positive and shared with them, we encouraged each other and set dates for coming for treatment."*

Women suggested two changes in the treatment model that could facilitate treatment for women in the community, (1) a decentralized treatment model that provides treatment in more rural health facilities, closer to homes, or a mobile treatment unit that moves periodically through communities and (2) transportation provisions or reimbursements, echoing the main barrier to treatment access.

Finally, a substantial number of women felt that greater awareness of or access to *screening* would increase uptake of treatment. Women suggested repeating screening in the communities for those who had missed earlier campaigns and increasing involvement of lay health workers, or community health volunteers, in outreach and education around screening.

Support from Peer Networks and Community Leaders

Women wanted to share their diagnosis with others in their community, both to be able to obtain psychological and financial support for treatment and to set an example. Most reported that privacy around their HPV status was not important to them.

> *"I am comfortable with any other person knowing my status because, he or she might be able to support me if am sick or I might be able to encourage and support a person who is sick but is too scared to receive treatment."*

A small minority of women who did not want to share their diagnosis with others, apart from their spouse or co-wives, gave reasons including a general desire for privacy about their own health, without specific mention of HPV or cervical cancer related stigma.

> *"The reason why I did not want anyone else to know is because some people tend to exaggerate things, if one hears you have this disease, they may start telling you how you have a very bad disease and that you will die soon"*

Women held contradictory opinions regarding the role of community leaders in facilitating treatment. Women who were in favor stated that leaders could "*mobilize women to seek treatment",* while those opposed feared a loss of privacy, stating that "*community leaders would spread rumors to the community members."*

Male Partner Involvement

Almost all women interviewed said the decision to seek treatment was theirs alone. However, they did feel like male support or opposition played a role in access of treatment services. Interestingly, most women stated that while men in general would likely not be supportive of their wives obtaining treatment, their own spouse had been. Reasons for other husbands' perceived lack of support were related to a lack of understanding or belief that HPV is a real threat, and low prioritization of their wives' health. Male support was generally described as financial support for transportation, with a minority naming encouragement or moral support for treatment. This could indicate either a false perception about a widespread lack of male support, or suggest that male support was a key factor in obtaining treatment (as all the women in this group had successfully obtained treatment).

> *"My husband support[ed] screening so that should I be confirmed positive, I start the treatment in time before it worsens…he provided me with fare and asked me to leave early so I can get to the hospital in time.*

> *"Some do not understand cervical cancer and some just care less about their wives and cervical cancer hence not becoming supportive. Other men are supportive when they value the lives of their female partners."*

A few women expressed concern about cultural and social beliefs regarding sexual activity that would prevent their husbands from supporting them through the recommended six week recovery period, or use of a condom afterwards. Some women even requested that a health provider speak with their husband.

> *"I had a concern with the issue of not having sexual contact with my husband for a month. We built a new house, which we are supposed to enter into in the course of this week. As Luos, we have our customs that we must uphold, what will I do?"*

Treatment and Empowerment

Many women expressed a sense of personal empowerment from either undergoing treatment or from gaining an understanding of the impact of HPV on their health as a key factor in overcoming barriers to treatment.

> *"I have come to seek treatment for a better future; I want a future so that I can continue taking care of [my children]"*

Finally, almost all women said they would recommend treatment to other women who they knew tested HPV positive, stating that the treatment was easier than they thought, free, quick and almost painless. Importantly, many felt that they had an important role to play as peer educators or advocates to convince other women who tested HPV positive to get treatment. Often, women expressed that their treatment experience changed their minds about privacy and the importance of sharing their experience.

> *"I never felt like letting anyone know about my treatment, now that I have, I can easily encourage my neighbor to seek for treatment in case she's positive."*
>
> *"I would tell her my experience about the treatment. How easy and how painless it is. How the doctors are prepared and how they talk nicely to us. I would tell her she has nothing to fear and she should gather courage and come."*

Discussion:

Follow-up for HPV-positive women is a critical component in cervical cancer prevention; the success of programs in LMICs is often limited by attrition between screening and treatment. This study used the CFIR framework to explore the contextual factors surrounding women's uptake of treatment after a positive HPV test in rural Kenya. We found that women were generally satisfied and even empowered by their treatment experience. The results also showed that the belief that the treatment they were seeking would have an important and positive impact on their health enabled women to overcome the barriers of fear, lack of transportation funds and distance to the treatment center.

These findings add substantially to a body of work that has primarily focused on structural, financial, and policy-related barriers and facilitators to the implementation of cervical cancer screening and treatment programs by exploring the patient experience from receiving results to navigating treatment access.[16, 17] The participant perspectives provide important insight into ways the treatment model can be improved. To our knowledge, this is the only study to assess patient-level factors impacting cryotherapy treatment in a low-resource setting using the CFIR framework. The use of a standardized framework is important to developing a sustainable and effective enhanced linkage to treatment strategy with the potential for replication in other settings.

The fact that empowerment associated with treatment emerged so strongly was encouraging and indicated a facilitating culture. However, substantial logistical and financial barriers remain in place for women in this model, despite free screening and treatment. Women traveled an average distance of over thirty kilometers and almost all women required some form of hired transportation. While the majority of women did not recall income loss, or reported a loss of less than 1000 Kenya Shillings ($10 US), the cost of transportation represented a significant burden, even among this group of women who were not lost-to-follow-up. Partner support was significant, and most often appeared in the form of payment for transportation. While almost all women stated that the decision to seek treatment was their own, their reliance on partners for financial support was crucial and may have important implications for future cervical cancer prevention and treatment initiatives. The frequency at which the costs of transportation to a distant treatment site and the reliance on partners were reported indicates a need to explore the decentralization of treatment with or without a mobile treatment unit, the use of transportation vouchers, or assistance of some type that emphasized transportation.

The use of peer educators to help encourage and facilitate treatment access may also be a strategy to overcome the logistical hurdles using an empowerment framework. While other studies have not shown educational interventions to be as effective as other implementation strategies for cervical cancer prevention,[18] peer-led counseling has increased perceptions of screening benefits and engagement in screening activities.[19, 20] Peer-to-peer education has played a large role in the success of HIV programs in this region, so participants were likely to have experience and comfort with this. Importantly, women saw themselves as potential peer educators, using their positive experiences with treatment to convince other women to get treated. In this way, the self-efficacy they displayed in obtaining treatment would be transformed into a sense of personal empowerment through a reflection of their own success and influence on others.

This qualitative data clearly elucidated points of clarification for the educational counseling provided throughout the outreach, screening and treatment activities. Although the current education modules stress that HPV is not cancer, some women continued to believe that a positive HPV result was synonymous with having cancer, which caused fears that sometimes resulted in inaction. Educational content and the mechanisms by which women are notified of their results should be rigorously tested to ensure clarity, as fear of cancer or more invasive procedures may prevent women from seeking appropriate treatment. In addition, these data highlight a need to address the misconceptions about family planning, infertility, and the need for medication as part of treatment both during outreach and at the time of screening and treatment. The persistent expectation that treatment would involve long-term medications may reflect an interpretation of medication as synonymous with treatment, as is the case with the more common diseases in the area: HIV, TB, and malaria. Based on these findings we updated the educational material to include more precise descriptions of the cryotherapy procedure and clarify that treatment does not require medication.

While this data highlighted crucial information that allows us to further understand how and why women are able to access treatment when free treatment is offered, there are limitations inherent to the study design. The current study is missing the voices and experience of women who were unable to access treatment, who were the majority of women screened. For example, in this population of women who had successfully accessed treatment, almost all were in a relationship or married, which was possibly a key factor in their success with navigating treatment. While the qualitative data suggests partner financial support was key in reaching treatment sites, we must identify and work with women who were lost-to-follow-up to fully begin to understand and address insurmountable barriers. In addition, as these interviews were done by the study team in proximity to treatment sites, there may have been some social desirability bias in responses related to treatment experience and provider respect.

Conclusions

These data provide valuable insight on the implementation of a community-based cervical cancer screening program through the perspectives of HPV-positive women who were able to access free treatment through referral to a county government hospital. While many women reported feelings of self-efficacy and empowerment, and were pleased with their experience deciding and accessing treatment, they represent the minority of patients. Despite multiple efforts to counsel women about the importance and availability of treatment, over half of the women who tested HPV-positive in the parent study did not access treatment. We have identified specific barriers and potential facilitators to treatment access that will inform new implementation strategies and ways to intensify efforts to reach the wider population of women who were lost-to-follow-up and work with health care teams to develop a linkage to treatment strategy that ensures greater follow-up with appropriate care.

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Availability of Data and Materials:
The datasets analyzed during the current study are available from the corresponding author on request. The codebook is included as supplementary material.

Competing Interests:
The authors declare that they have no competing interests

Author Contributions:
MJH is the overall study PI. She conceived the study, led the study design, led the coding and analysis, and wrote the manuscript. KA, SY and SI assisted with the coding, analysis and conceptual framework. SY lead data collection activities. SI led data management. EB assisted with the manuscript preparation and acts as the site PI. All authors have read, actively edited and approved the final version of the protocol.

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Table 1: Refined CFIR constructs and key findings regarding HPV-positive women's experiences with a referral-based cryotherapy treatment strategy

Construct	**Topics Covered**	**Key Findings**
Intervention Characteristics		
Relative Advantage	• What are the advantages of the proposed treatment model?	• Offered free of charge, outpatient
Adaptability	• What are other models of treatment that would facilitate increased access? • What are factors of the current treatment model that could be improved?	• Decentralized treatment or transportation support would improve the model
Complexity	• Perceptions of treatment feasibility and sustainability • What is the participant's understanding of the screening and treatment cascade?	• Women had unanswered questions after treatment, regarding follow-up, need for medication or potential impact on fertility
Outer Setting		
Patient Needs and Resources	• What can the health facilities do to facilitate patient treatment acquisition?	• Provider respect was high
Inner Setting		
Culture	• What is the level and impact of male support? • How could community leader involvement facilitate treatment?	• Male financial and moral support were important to treatment acquisition • Many were concerned about post-treatment abstinence or re-infection • Ambivalence about community leader involvement
Access to Knowledge & Information	• How can outreach and education strategies be improved? • How does peer education and support impact treatment acquisition?	• Peer education noted in both educating about screening and encouraging treatment
Characteristics of Individuals		
Knowledge & Beliefs about the Intervention	• Did women understand the meaning of a positive HPV result? • Did women understand the process and availability of treatment? • Do women understand the importance of treatment for their health?	• Role of HPV in development of cancer was well understood, however some women equated an HPV positive result with cancer • Women knew that early treatment would be simpler than treatment for advanced disease
Self-efficacy	• Do women prioritize accessing treatment for their health? • How do health beliefs and self-efficacy impact women's ability to overcome barriers to treatment?	• Women felt knowing HPV status allowed them to move on a health action (treatment) • Treatment had an empowering influence • Post-treatment, women felt that they could/should be role models
Individual Stage of Change	• What role do peer networks or social support play in treatment access? • What role do individual health beliefs play in reactions or decisions about treatment for a positive HPV test?	• Women felt relief at knowing HPV status • Fear surrounding HPV result and association with cancer led to some inaction

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Final RO1 Treatment Codebook

Nodes

Name	Description	Files	References
Barriers to Accessing Treatment		50	56
Cost & Money		168	199
Distance		104	111
Fear or Anxiety about scope of Procedure		54	58
Health Beliefs		7	7
Logistical barriers		39	41
Social Opposition		0	0
Friends-Relatives-Peer Opposition		5	5
Partner Opposition		28	30
Transport		128	143
Community Leader Involvement		213	218
Facilitators to Treatment Access		26	27
Financial Empowerment		18	18
Increase CHV Involvement		17	17
Increase CHV Involvement		18	18
Logistical Changes		3	3
Additional Treatment Staff		5	5

Name	Description	Files	References
Appointment Reminders		10	10
Financial Incentive		49	53
Phone Call or SMS		64	65
Transportation		146	162
Treatment Center Proximity- Make it closer- Change in Treatment Center (2)		275	341
Mobilization and Awareness-Sensitization		168	190
Peer Education		120	142
Social Support		5	5
Friend-relative-peer support		26	27
Partner Support		97	110
Knowledge Gained from Positive HPV Test and Treatment		105	114
Health Outcomes & HPV Specific Facts		285	379
Male Involvement		31	32
Male Opposition		95	109
Difficulty Maintaining Abstinence for One Month		26	26
Stigma		15	15
Male Support		408	481
Memorable Quotes		36	40
Myths and Misconceptions		67	79

Name	Description	Files	References
Perceptions on Receiving an HPV Positive Test		31	32
Negative		278	322
Positive		301	341
Privacy		39	39
Important		105	109
Not Important		159	162
Recommendation for Treatment After HPV Test		1	1
No		1	1
Yes		511	556
Strategies to Improve Treatment Experience		44	47
Improve Communication between Study Team and Participants		40	41
Provider Attitude		51	52
Treatment Experience		4	4
Negative Experiences		22	23
Embarrassment		3	3
Privacy		8	8
Positive Experiences		109	124
Provider Attitude		85	89
Treatment Explanation		0	0
Adequate		94	98
Inadequate		72	77

Name	Description	Files	References
Unanswered Questions		377	687
Uncategorized Themes		113	139

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BMC Cancer

STUDY PROTOCOL Open Access

Study protocol for a cluster-randomized trial to compare human papillomavirus based cervical cancer screening in community-health campaigns versus health facilities in western Kenya

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Abstract

Background: Despite guidelines for cervical cancer prevention in low-resource countries, a very small proportion of women in these settings undergo screening, and even fewer women are successfully treated. Using pilot data from western Kenya and World Health Organization recommendations, we developed a protocol to implement evidence-based cervical cancer screening and linkage to treatment strategies to the rural communities. We describe the protocol for a cluster-randomized trial to compare two implementation strategies for human-papillomavirus (HPV)-based cervical cancer screening program using metrics described in the RE-AIM (reach, efficacy, adaption, implementation and maintenance) framework.

Methods: The study is a three-year, two-phase cluster-randomized trial in 18 communities in western Kenya. During Phase 1, six control communities were offered screening in health facilities; and six intervention communities were offered screening in community health campaigns. Screening was done with human-papillomavirus testing through self-collected specimens. Phase 1 ended and we are working in partnership with communities to further contextualize the implementation strategy for screening, and develop an enhanced linkage to treatment plan. This plan will be tested in an additional six communities in Phase 2 (enhanced intervention). We will compare the reach, efficacy, cost-effectiveness and adaptability of the implementation strategies.

Discussion: Effective low-cost cervical cancer prevention technologies are becoming more widely available in low- and middle-income countries. Despite increasing government support for cervical cancer prevention, there remains a sizeable gap in service availability. We will use implementation science to identify the most effective strategies to fill this gap through development of context-specific evidence-based solutions. This protocol design and results can help guide implementation of cervical cancer screening in similar settings, where women are most underserved and at highest risk for disease.

Trial registration: This trial is registered at ClinicalTrials.gov, NCT02124252.

Keywords: Cervical cancer screening, Community health campaigns, Kenya, HPV self-collection, Implementation science

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Background

Despite the fact that cervical cancer is highly preventable through vaccination and organized screening programs, over 500,000 women worldwide are diagnosed with the disease every year [1]. About 9 out of 10 cervical cancer deaths occur in low-resource countries, with a particularly high burden in sub-Saharan Africa, where the mortality rate is 85% [2, 3]. The inequality between high and low-resource countries is mainly due to lack of screening in low-resource countries, which lack the health care infrastructure required for the cytology-based screening programs that have dramatically reduced the disease burden in wealthier countries. The World Health Organization (WHO) recommends alternative cervical cancer prevention techniques and protocols for low-resource countries that employ low-cost or simple-to-use screening technologies [4]. One such strategy – high-risk human papillomavirus (HPV) testing– has been shown to reduce the incidence and mortality from cervical cancer when coupled with outpatient treatment for women with HPV-positive results [5].

In addition to effective screening tools, the impact of cervical cancer prevention programs depends on two main context-specific factors: (1) women's access to screening and (2) successful acquisition of treatment for women who screen positive. Access to both screening and treatment is most challenging in poor rural areas, due to geographic and infrastructure constraints [6, 7]. Most health care in rural areas takes place in small health facilities with limited space, staffing, and equipment, making it challenging to implement same-day "screen & treat" strategies that have been proposed to overcome barriers to treatment access [8]. So, despite the development of guidelines for cervical cancer screening that employed evidence-based technologies and lower resource protocols, the lack of rigorously tested, context-specific implementation strategies has left a gap between policy and practice.

In order to develop a context-specific, sustainable implementation strategy, we undertook formative work to identify local barriers and facilitators for cervical cancer screening in government-supported health facilities in rural western Kenya, an area of East Africa with a high cervical cancer burden and screening rates as low as 3% [9, 10]. We found that access to screening was limited by lapses in service availability and lack of clinic attendance for preventive care [11]. When services were available, both providers and patients found the need for a pelvic exam limited the acceptability of cervical cancer screening. Based on the facility-based barriers, we developed and piloted a highly successful community health campaign model for screening, consisting of outreach followed by a brief campaign held in a central site in the community, offering on-site screening and referrals for treatment [12]. An advantage of community-based screening is that only screen-positive women need to visit health facilities for follow-up care, reducing the visit burden for both woman and facilities, and allowing resources to be directed toward strategies to increase treatment uptake, such as intensified follow-up, transportation assistance or mobile units that bring treatment to remote villages. Thus, as has been seen in other health services [13–15], by combining community-screening with enhanced linkage strategies, our approach could maximize the health impact by increasing the number of women screening *and* the proportion successfully accessing treatment.

To address the reluctance around pelvic exams, we chose to offer screening with self-collected specimens for HPV testing, an evidence-based strategy that would eliminate pelvic exams for initial screening, further increasing screening acceptance and efficiency. We developed a study protocol that will allow us to compare two context-specific implementation strategies for an HPV-based cervical cancer prevention program through a cluster-randomized trial of HPV-based cervical cancer screening in community-health campaigns versus health facilities using the RE-AIM framework [16, 17]. This paper describes the study protocol (V 3.0, 20 July 2017) and the plan to evaluate the adaptability, comparative effectiveness and cost-effectiveness of these two strategies.

Methods

Study design and setting

The study is a two-phase cluster randomized trial in western Kenya to evaluate reach, effectiveness, cost-effectiveness and maintenance of two implementation strategies for a cervical cancer prevention protocol that consists of four critical, evidence-based components:

(1). **HPV and cervical cancer outreach and education**. In western Kenya, we found that women's baseline knowledge and perception of cervical cancer risk is low; a brief educational intervention provided by community health workers in primary care clinics improved these baseline factors and increased women's intention to screen [18].

(2). **HPV-testing using self-collected specimens with referral for treatment based on a single positive result.** An HPV-based screening strategy is effective at reducing incidence of cervical pre-cancer and invasive cancer when women with screen-positive results undergo cryotherapy [5, 19, 20]. Self-collected specimens are highly accurate, with comparable results to provider-collection for the detection of high-grade cervical precancer [21–23] Women have consistently found self-sampling acceptable and preferable to provider-testing [24–26]; this finding has been supported in studies from sub-Saharan Africa [27, 28]. Studies in various countries have shown that a self-collection strategy increases screening uptake by women not attending clinics [29–34].

(3). **Notification of screening results using text messaging.** Based on our prior experience with mobile health interventions [35, 36] and the high rates of cell phone use in western Kenya [37], HPV test results were sent to all women via text message with instructions about appropriate follow-up as recommended by the Kenya Ministry of Health guidelines.

(4). **Treatment with cryotherapy unless contraindicated by cervical exam.** Cryotherapy is a low-cost, effective treatment method that can be safely carried out by mid-level providers in low-resource settings [38, 39]. Women who are not candidates for cryotherapy (i.e. lesions too large or abnormal cervical anatomy) were offered Loop Electrosurgical Excision Procedure carried out in the County Hospital. Together, HPV testing followed by cryotherapy for women who test positive reflect the current WHO recommendations [40].

In Phase 1 of this study, we compared two implementation strategies that incorporated these four evidence-based elements of screening. Based on our preliminary data, we found that reaching and attending a health facility for preventive care was a significant barrier to screening for many women. Therefore, the main objective was to compare a model offering screening in brief, high throughput community health campaigns to that of a standard of care in which screening was offered in local health facilities using the metrics defined in the modified RE-AIM framework.

In Fig. 1, we present an overall schema of the cluster-randomized trial. In Phase 1, six communities were randomized to the intervention: HPV screening carried out in **community health campaigns**. The remaining six were comparison communities: HPV testing offered in **government health facilities**. HPV-test positive women in all communities were referred to the County hospital for immediate treatment, which is considered standard linkage to treatment.

Development of an enhanced strategy for linkage to treatment: After Phase 1, we have an "inter-phase intervention development" period in which we are evaluating the results from the trial. The outcomes from the qualitative and quantitative measures will be used to refine the screening intervention using context-specific details and develop an enhanced strategy for linkage to treatment. Although we have identified factors that enable and inhibit women's access to treatment, we chose to wait until after Phase 1 for the development of the enhanced strategy for linkage to treatment in order to truly work in partnership with the community. The delayed development of the linkage to treatment strategy has allowed us obtain a baseline measure of the efficacy of standard referrals and identify factors that would influence women's access to care in this setting.

After developing the strategy for enhanced linkage, we will pilot and then test the linkage to treatment strategy as part of an "enhanced intervention" in the six communities that served as controls in Phase 1. Using these communities for the enhanced intervention increases the efficiency of the study in two ways: i. we will have done community enumeration and engagement, and ii. we will compare linkage to treatment outcomes from these "enhanced intervention" communities to the intervention communities from Phase 1.

Study activities

Study preparation

- **Community enumeration and randomization:** Prior to the initiation of the cluster randomized trial, we characterized the study communities using a combination of census data, health facility

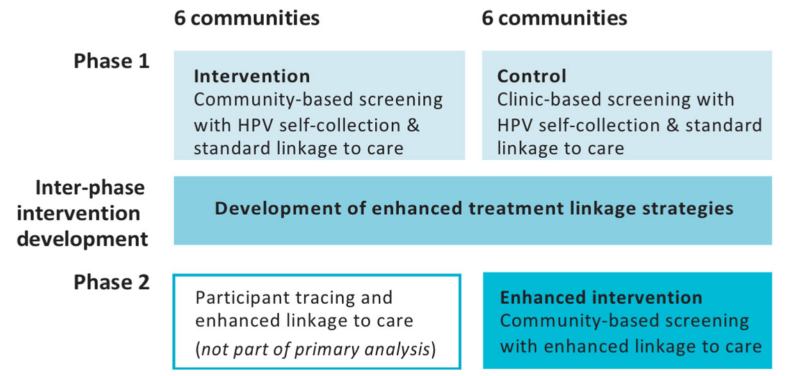


Fig. 1 Two-phase cluster-randomized trial design

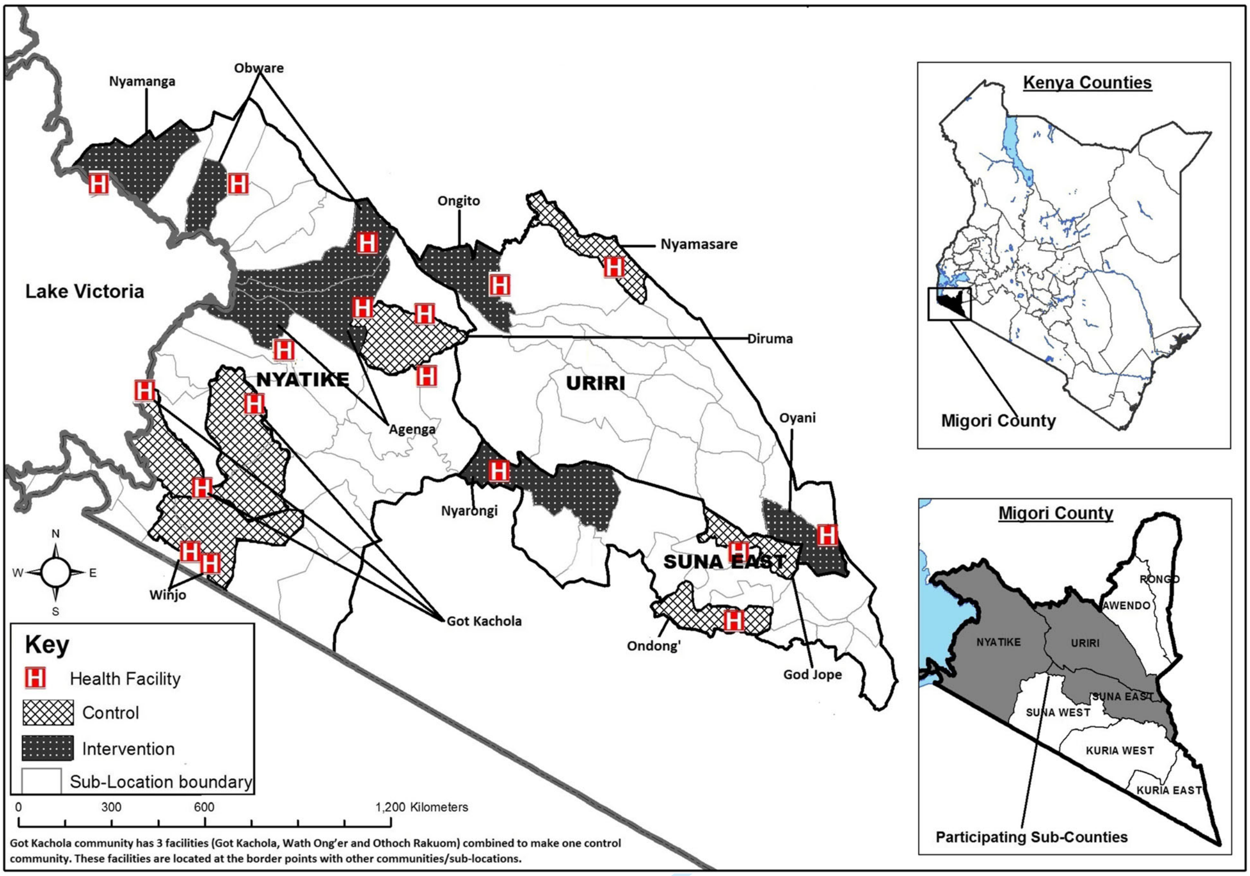
information, mapping and prospective demographic data. We identified communities of approximately 7500 people in three sub-counties of Migori County in western Kenya (population: 350,000, 65 government health facilities). Population estimates were calculated using the 2009 Kenyan census data with population growth estimates for 2015 and 2014, a method that was validated through door-to-door enumeration for a recent large-scale community randomized trial in rural western Kenya [41]. Eligible communities had at least one government health facility with capacity to provide HPV testing, support from community leaders for the community outreach and/or health campaigns, accessibility to health centers via a maintained transportation route and sufficient distance from other potential study sites to limit contamination between arms (buffer zones). As our target group is women in rural communities, we excluded urban settings or communities in which the nearest health center is Migori County Hospital and those that were taking part in a cluster-randomized trial of large-scale community-health campaigns for HIV-testing [41]. We conducted unmatched randomization using a random number generator on Stata 10. The unmatched design will allow us to consider the relationship between community-level factors and our outcomes of interest. After communities were chosen, population estimates were refined through household enumeration done by community health workers assigned to villages and sub-locations within the communities.

- **Provider and key stakeholder focus groups:** Clinicians and community health workers ("providers") within the community health campaigns and health facilities participated in focus group discussions to provide baseline data about perceived barriers and strategies to facilitate HPV screening uptake during the planning and implementation adaptation period of the study. Although we sought key stakeholder input throughout the development of the implementation strategies, we held three focus group discussions with key stakeholders in the intervention and control communities for Phase 1 (community chiefs, leaders of women's groups, reproductive health coordinator, medical superintendent and Charge Nurse of Migori District Hospital). The goals of these focus groups were to obtain a group perspective on the intervention as planned for their communities, any anticipated challenges and strategies to optimize the screening strategy in both arms. Focus group discussions were analyzed using the theoretical domains framework, which mapped behaviors to intervention strategies, using evidence-based principles of behavior change [42].
- **Training and finalization of the screening protocol.** We used educational modules piloted in western Kenya to provide standardized training in cervical cancer counseling and HPV-self testing to community health workers and clinicians [43]. The community health workers received training in community outreach messaging, delivery of the educational module in the community health campaign setting, and teaching women how to perform self-collection of HPV specimens. In addition to the general training, clinicians had undergone Ministry of Health-supported training to learn the cervical cancer screening protocol, including follow-up and pre-treatment exams. Two nurses who had undergone cryotherapy training were identified and supervised for ten cryotherapies at the County Hospital prior to study initiation.

Cluster randomized trial: Phase 1

After community enumeration, training and protocol finalization, we launched the cluster-randomized trial in the six control and six intervention communities in Migori County. (Figure 2) Phase 1 of the trial, consisting of the activities listed below, took place over the course of 1 year.

- **Outreach and education:** In all communities, information about cervical cancer screening and the opportunity to learn more about HPV-based testing were provided through community outreach, including fliers, posters and brief informational sessions in markets, churches and women's group meetings. Women and community leaders were provided with information on how to access cervical cancer screening in their community, e.g. location of clinic or timing and location of community health campaign. In all communities, women were invited to participate in a brief, standardized cervical cancer education module, either at the health campaign or in the health facility. The module is approximately 15 min and covers topics ranging from simple anatomy, definition of cervical cancer and HPV, how screening works, what treatment is available for precancerous lesions, and how to perform HPV self-testing.
- **Community-based testing (intervention group):** In six communities randomized to community-based HPV testing, community outreach teams carried out two-week community health campaigns in which HPV-testing was offered through self-collection. In order to reach the entire community, the campaign moved to multiple sites over the two-week period,



Got Kachola community has 3 facilities (Got Kachola, Wath Ong'er and Othoch Rakuom) combined to make one control community. These facilities are located at the border points with other communities/sub-locations.

Fig. 2 Map of communities randomized to control and intervention activities in Migori, County Kenya. This map was developed by Easter Olwanda, who has provided written permission for use in this publication

with approximately one to 2 days at each site. The campaigns consisted of health education and informed consent, after which a health worker provided additional instructions about self-collection and recorded a mobile phone number before dispensing the HPV testing kit. The woman then would go to a private area in the campaign tent to self-collect the specimen and returned the completed collection kit to the health worker prior to leaving.

- **Clinic-based testing (comparison group):** In the six communities randomized to the control arm (clinic-based testing), women were directed through community outreach to go to their local health facility during regular clinic hours to carry out screening. At the clinic, a health worker offered the educational module, obtained informed consent and provided additional information about self-collection, and recorded a mobile phone number before dispensing the HPV testing kit and instructions.
- **HPV testing:** While HPV test results are not the primary outcome for this study, the accuracy and reproducibility of measurements are essential for outcomes in both arms and for modeling the impact of the implementation strategies in larger populations. We tested the DNA for 14 HPV types (16, 18, 32, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68) using CareHPV™ testing system. Collected specimens were transported daily from the CHCs and weekly from the health facilities to the study lab at Migori County Hospital. Tests were run in batches of 90, with a turnover time of approximately 1–2 weeks for results.
- **Notification of HPV results:** HPV test results were preferentially sent to women via text message with instructions about appropriate follow-up as recommended by the Kenya Ministry of Health guidelines. Messages were developed by key stakeholders and women from the target population during the focus group discussions. Women who did not have access to a phone, or did not wish to receive their results by SMS could opt for a return visit to the clinic, or a home visit.
- **Standard referral for treatment (both arms, Phase 1):** Women who were HPV-positive were

referred to Migori County Hospital for a visual exam with acetic acid and treatment with cryotherapy per the WHO guidelines [44].

- **In-depth participant interviews and focus groups:** We conducted semi-structured interviews with randomly selected participants in both arms at three key points in the cervical cancer prevention cascade: screening delivery (*n* = 30), notification of results (n = 30) and treatment access (all). Participants were contacted either in person or by phone, and interviews conducted in person by experienced qualitative interviewers in the local language using interview guides developed by the research team. Topics explored in these interviews will elucidate ways to make cervical cancer screening more acceptable and accessible to women. Interviews captured quantitative data about women's participation in various aspects of the prevention cascade. Interviewers then explored women's perspectives of their experience with the intervention and explanatory factors related to the decisions to access screening and treatment through open-ended questions. Among women who did not access treatment, we probed for factors or strategies that would allow them to link to care in the future.
- **Provider and key stakeholder interviews and focus groups:** During the cluster- randomized trial, providers in the community health campaigns underwent brief interviews at two time points: after three and six campaigns had been completed. In the clinic-arm, providers underwent interviews at three, 6 and 12 months into the intervention. These interviews will help to understand explanatory factors for the success or failure of the intervention from a health system perspective. Interview topics included personal attitudes and beliefs around screening importance and feasibility, perceived and actual barriers to implementation and potential strategies to overcome provider, health delivery and patient-level barriers to screening and treatment.

Intervention development and cluster randomized trial: Phase 2

- **Enhanced linkage to treatment:** We will work with health care providers, community members and other stakeholders to review outcomes from the quantitative, qualitative and process measures in Phase 1, critically examine and modify the cervical cancer *screening* strategy to develop and pilot the enhanced linkage to *treatment* intervention over a 6–9 month period between Phase 1 and 2. We will do this through a series of key stakeholder meetings, followed by the establishment of smaller working groups for the creation of the specific intervention components. In the first set of meetings, we will present the findings from Phase 1 and seek feedback on representativeness and discuss implications for culturally relevant intervention strategies. Options for the most feasible and acceptable strategies to increase the number of women linking to treatment will be explored in the light of that data.

Criteria for potential strategies include: community-developed, low-cost, feasible in all study communities, and able to ensure treatment for HPV-positive women in a timely manner in accordance with Ministry of Health guidelines. In a second, small stakeholder meeting, we will review potential strategies discussed and developed in the first meeting, and discuss solutions proposed in other settings, including the use of mobile treatment units, transportation vouchers, and treatment "navigators" to help women understand and travel to treatment sites. Once the linkage intervention has been defined, we will hold another working group with stakeholders to create a standardized protocol, training manual, standard operating procedures and data collection instruments. After equipment procurement, provider training and further outreach messaging, the enhanced linkage strategy will be piloted in two to three Phase 1 intervention communities prior to launch of Phase 2.

Implementation framework

The study design, and outcome measures are centered in the essential implementation metrics as defined by the RE-AIM framework, which modified to the context of our study (Table 1) [17]. Outcomes will be evaluated through quantitative, qualitative and process measures. This design will allow us to test the following hypotheses:

- Community-based cervical cancer screening will reach a larger portion of eligible women and be more acceptable to patients and providers than clinic-based testing. (REACH)
- A community-driven intervention will improve linkage to treatment among women who need treatment after an HPV-positive screening test compared to standard referral. (EFFICACY)
- We will identify modifiable patient and health system challenges that can be addressed to make health campaign based HPV testing and enhanced linkage to treatment succeed and be sustainable. (ADOPTION & MAINTENANCE)
- Community-based cervical cancer screening with enhanced linkage to treatment will have a greater population-level health impact as measured in women reached with screening and any necessary treatment, and favorable cost-effectiveness profile

Table 1 A modified RE-AIM framework to evaluate community health campaign-based cervical cancer screening compared to health-facility based screening

	Dimension Goal	Implementation Question	Hypothesis
Reach	Who is intended to benefit? How do we reach them?	How do we reach reproductive-aged women in rural kenya?	A screening strategy offered through community health campaigns in a central location will reach a large proportion of reproductive-aged women.
Effectiveness	Is the program effective?	Are women getting screened for cervical cancer with HPV?	A community-based strategy allowing for self-testing will be highly acceptable.
	How do we ensure effectiveness?	Are HPV + women successfully linking to treatment?	Innovative, patient and provider-designed strategies will increase the number of women linking to care.
Adoption and Maintenance	How can strategy be maintained after initial implementation and adopted in similar communities?	What are the patient, provider and delivery system processes necessary to ensure consistent service provision?	A screening protocol with a simple, patient-performed test offered as part of a health fair will minimize the costs to the health care system to introduce screening.
	What are the short and long-term health effects in the community?	What is the population-level health impact of screening using HPV self-testing in the CHCs with enhanced linkage to care?	The high number of at -risk women reached through the CHC-base strategy with enhanced linkage to care would produce a greater population-level health impact.
Implementation	What is adherence to the implementation strategy at the delivery level? What are the costs of implementation?	Is HPV testing being offered and delivered consistently at the CHC and clinic sites? What is the cost per lesion treated?	Providing testing in a high-volume CHC will reach a large number of women with low staffing and infrastructure needs, and will therefore have a lower cost per woman treated than a standard strategy.

compared to clinic-based strategies and standard referral for treatment. (IMPLEMENTATION)

Participants

Our target population is women living in rural Kenya who are eligible for and would benefit from cervical cancer screening per the Kenya Ministry of Health Guidelines (25–65 years old with an intact uterus and cervix). The study population is women 25–65 years in the twelve communities in the Nyanza Province who access screening during both phases of the trial.

Recruitment and consent

Communities participating in the trial provided verbal assent in the planning process with written consent obtained from individuals for screening. Participants were recruited through the community health campaigns and in the clinics. Women within the target age range were invited to attend the cervical cancer educational module. After the health talk, women were asked to provide informed consent by research assistants for a post-module questionnaire and follow-up after screening completion. Women who were not willing to provide informed consent were still able to attend the health talk and have access to the HPV screening strategy assigned to her arm, but were not contacted for the follow-up in-depth interviews or participation in focus group discussions.

Primary and secondary endpoints

To determine the **reach** of cervical cancer screening using HPV-testing in community health campaigns compared to clinics, we are using the following metrics: i) the absolute number of women who completed screening in each arm and ii) the proportion of women in each arm who completed screening. The total number of women in each arm is the number of women 25–65 in each community as determined by census data. Secondary outcomes will include iii) the proportion of women who accept screening among women offered at each site and iv) the proportion of women in the clinic-based arm who request clinician-collected specimens.

To determine the **efficacy** of a community-developed strategy to increase treatment access, we will compare the efficacy of the community-based HPV testing with standard versus enhanced linkage to treatment using the following metrics: i) the number of women who receive treatment after screening HPV + in the intervention (Phase 1) compared to the enhanced intervention (Phase 2) and ii) the proportion of HPV-positive women in each arm who complete treatment. Secondary outcomes that address quality of care concerns for the models will include iii) the proportion of women who receive the correct treatment (per Ministry of Health protocol) during a single treatment visit and iv) the average time between HPV testing and access of treatment by arm.

Data collection

We collected data on both screening and linkage to treatment from both control and intervention communities in Phase 1. Data was collected by members of the research team and entered into pre-programmed tablet computers using OpenDataKit software (ODK™),(https://

opendatakit.org) which had been used by this research team for the past several years. Programming included checks for range, structure, and internal consistency. During the community-health campaigns, data was collected directly from providers and participants into the tablets and was transferred daily via a secure electronic transfer to our data center facility in Kisumu, Kenya and stored on a secure server. To capture visits and outcomes from clinic-based screening and facility treatment, a member of the research team visited each clinical facility on a weekly basis to enter data from Ministry of Health registers and study-specific forms into the tablets. Data transfer from clinical-sites took place weekly. The same data collection procedures will be applied in Phase 2.

Implementation consistency

All four basic components of the intervention (outreach/education, HPV-testing, notification of results and linkage to treatment) were monitored throughout Phase I of the trial to ensure maintained fidelity to the protocol and quality of service and message delivery. Quantitative outcome measures, as well as the process measures listed below assessed continued fidelity of the intervention as offered. Qualitative data from in-depth interviews, focus-group discussions and process measures will provide a more complete picture about subtle but important factors that may influence the actual service delivery and uptake.

Sample size

Using estimates from the 2009 Kenya census [45] with projected population growth for 2015 and results from recent community-wide census enumeration carried out by a cluster randomized trial in an adjacent district [46], we have estimated the total available population of women to be approximately 1000 per community of 5000. The estimates for attendance at community health campaigns (60% or 600 women) and clinics (30% or 300 women) and screening uptake were based on our formative work, community health campaign attendance in adjacent districts, and prior studies of self-collected HPV testing [27, 28, 47]. Our assumptions were that (1) attendance would be higher at community health campaigns and (2) screening uptake would be higher among women attending community health campaigns because most women attend based on outreach messaging around cervical cancer. These assumptions suggested a study population of 510 women per community accessing testing through community health campaigns and 210 accessing screening through clinics. For Phase 1, the total number of women accessing screening in the six communities randomized to community health campaigns would be 3060 and 1260 in communities randomized to clinic-based testing. We used these conservative estimates for sample size calculations (see below), but allocated resources for up to 4500 women in the community-testing arm and 2000 women in the clinic-based screening arm to ensure continuity of study activities. We also enrolled all providers and targeted key ministry of health stakeholders for quantitative and qualitative assessments of barriers and facilitators to care. A representative subset of this group were invited to participate in meetings to develop the enhanced linkage intervention.

Statistical analysis

- *Preliminary Analysis:* For each outcome, we will produce descriptive statistics (frequencies, proportions, etc.) overall, across clusters of interest (community, clinic, provider, etc.), and over time. We will also graph these data to identify visual trends.
- *Primary and Secondary Analysis:* Although this is a community-level intervention, the main outcomes will be analyzed at the individual level. We will compare the number and proportion of women who screen for HPV (reach) and who get treated for a positive HPV test (efficacy) in communities assigned to community vs. clinic-based testing using generalized estimating equations to account for the correlation among observations within communities. Efficacy: We will employ a log link and Poisson distribution with an offset term to represent the size of each community.
- *Power calculations:* We anticipate being able to observe a 30% difference in overall screening uptake between the control and intervention arms, a conservative estimate relative to previous cluster randomized trials. The power calculations assume an alpha of 0.05, a beta of 0.20, and an intracluster correlation coefficient of 0.072 for screening and 0.11 for treatment, based on calculations from a cluster-randomized trial of HPV efficacy [5].

Cost-effectiveness analysis (maintenance)

We assessed the costs, population health impact, and incremental cost effectiveness of three intervention strategies (clinic-based screening with standard linkage to treatment; community screening with standard linkage; and will assess community screening with enhanced linkage). To do this, we undertook a micro-costing of the resources needed to carry out the activities in both arms in Phase 1 and 2. Costing included 1) personnel (including fringe benefits); 2) recurring supplies and services; 3) capital and equipment; and 4) facility space. Intervention costs were assessed using a uniform cost data collection protocol to quantify resources used and associated costs in each of the study sites (community-health campaigns, clinics, laboratories and district hospitals). Data was obtained through administrative record review and interviews with administrative, finance and human resources staff, supplemented by direct observation in a limited number of staff "time and motion" studies in order to distinguish cervical cancer-related activities from other health services delivered by the same personnel. Costs were summarized as total program costs as well as costs per woman screened and per HPV positive women treated.

We observed study outcomes to estimate the health outcomes associated with each screening and linkage strategy. Observed data include will include the number of women screened and treated for high-risk HPV, the proportion of women undergoing cryotherapy vs. LEEP, and the side effects associated with each treatment. We will find the best possible available data to estimate the prevalence of various HPV-subtypes in the region, and the associated risks of cervical intraepithelial neoplasia (CIN), recurrence rates of CIN after treatment, and invasive cancer in women with and without treatment. We will translate each health event into a standard metric of burden of disease, Disability-Adjusted Life Years (DALYs), which combines morbidity (and associated disability) with premature mortality (lost "life years").

We will use the micro-costing described above to estimate several indices comparing costs to desired program outcomes: cost per case of HPV detected; cost per case of CIN detected; cost per woman successfully linked to facilities for treatment; and cost per woman treated. We will construct a decision model to estimate the health impact of HPV screening and linkage to treatment in a population cohort of 1000 women. This model will explicitly portray the paths from HPV to detection (by clinical presentation or screening), the risks of clinical progression, and outcomes with and without treatment (early or late). It will incorporate data on local epidemiology (HPV prevalence and cervical cancer, from Phase 1 and existing surveillance data); the clinical course of HPV and cervical cancer (from scientific literature); and the effectiveness of treatment (with cryotherapy and LEEP, as well as for more advanced disease, from scientific literature). Model outcomes will include deaths from cervical cancer, lost years of life, and morbidity (short and long-term), and DALYs (disability adjusted life years).

We will use the decision-analysis model to assess the incremental cost-effectiveness ratio (ICER), defined as the added cost per DALY averted, when comparing intervention strategies. We will also calculate the ICER compared to the current standard, which is no organized available screening, using baseline data of screening availability and use to calculate this. We will also estimate the costs for scaled-up replication, which will include variations in the number of and costs for personnel, community-health campaign structure and duration, HPV screening test costs laboratory costs and different linkage strategies.

Process measures

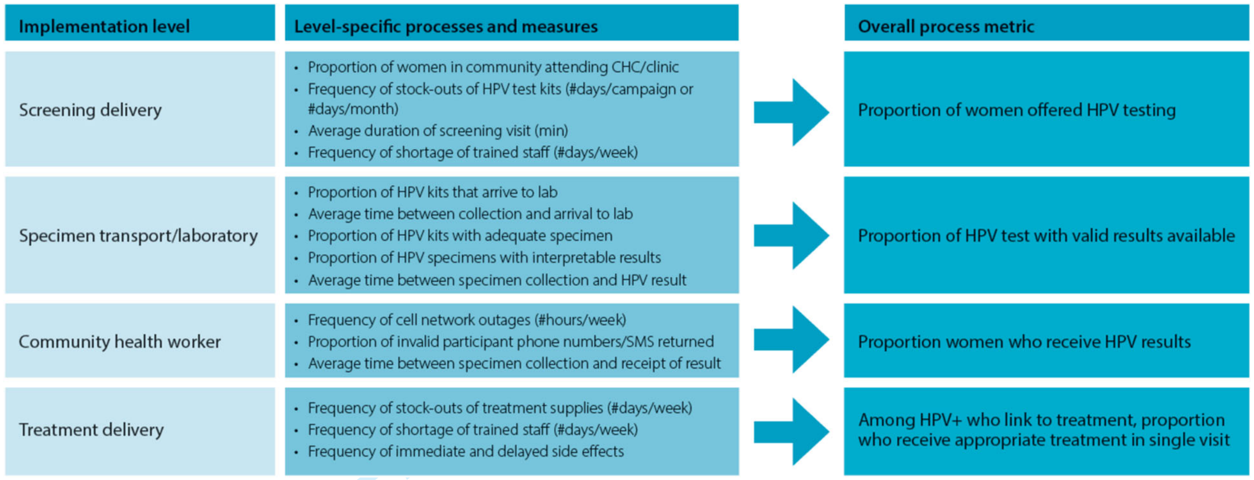
We will use quantitative process analyses to evaluate the strategy implemented in both arms at four levels of the intervention delivery process (Fig. 3). These include a) the proportion of women from each community health campaign offered HPV testing or referral (community health campaign-level processes); b) the proportion of HPV tests for which valid results are available (specimen transport and laboratory processes); c) the proportion of women who receive their test results (community health worker processes); and c) the proportion of HPV+ women attending a treatment visit who receive the appropriate treatment per Kenya Ministry of Health guidelines (health delivery center processes). We will use data from the provider and participant interviews and focus groups to explore the factors impacting the relevant service delivery processes that affect the overall result though quantitative and qualitative measures as well as explore additional key barriers and facilitators to both screening and treatment. Focus group data will enrich these conclusions and be used to develop an enhanced linkage intervention.

Ethical review

The trial was reviewed by an implementation and dissemination science section at the National Cancer Institute prior to funding. Ethical approval was obtained by the Committee for Human Research at the University of California, San Francisco (#14–13,698), Duke University Institutional Review Board (Pro0007742), and the Scientific and Ethical Review Unit at the Kenya Medical Research Institute (SERU 2918). Any major protocol changes will be communicated to all three review boards and to the trial registry at ClinicalTrials.gov. Complete trial registry data is available in a Additional file 1.

Trial status

Focus Group Discussions and in-depth interviews with key informants took place in August and September 2015. A pilot campaign took place in December 2015. Screening activities and enrollment in Phase I of the cluster-randomized trial were carried out between January and September 2016. We are now sharing feedback of Phase I results and observations with various stakeholders (community members, health care providers, and health management teams) in preparation for FGDs and working groups, which are aimed at enabling us design a strategy for enhanced linkage to treatment.



Implementation level	Level-specific processes and measures	Overall process metric
Screening delivery	• Proportion of women in community attending CHC/clinic • Frequency of stock-outs of HPV test kits (#days/campaign or #days/month) • Average duration of screening visit (min) • Frequency of shortage of trained staff (#days/week)	Proportion of women offered HPV testing
Specimen transport/laboratory	• Proportion of HPV kits that arrive to lab • Average time between collection and arrival to lab • Proportion of HPV kits with adequate specimen • Proportion of HPV specimens with interpretable results • Average time between specimen collection and HPV result	Proportion of HPV test with valid results available
Community health worker	• Frequency of cell network outages (#hours/week) • Proportion of invalid participant phone numbers/SMS returned • Average time between specimen collection and receipt of result	Proportion women who receive HPV results
Treatment delivery	• Frequency of stock-outs of treatment supplies (#days/week) • Frequency of shortage of trained staff (#days/week) • Frequency of immediate and delayed side effects	Among HPV+ who link to treatment, proportion who receive appropriate treatment in single visit

Fig. 3 Quantitative process measures for four aspects of cervical cancer prevention program delivery

Discussion

Substantial progress toward cervical cancer prevention has been made through research validating low-cost screening strategies that have been included in national and international protocols and guidelines. However, like many international guidelines, the WHO cervical cancer guidelines lacks advice on active implementation strategies [48]. While this is partly due to an emphasis on the clinical portion of the guidelines, some of this can be attributed to the lack of effective implementation strategies. Our goal with this novel study is to work with the community using a rigorous implementation framework to develop a strategy that could be scaled to improve the reach and efficacy of cervical cancer prevention programs in rural Africa, where the lack of health care infrastructure and services has lead to poor health outcomes. We are also hoping that the methodology of this project can be expanded to develop implementation strategies that would help address other health care needs.

Based on our formative work, we expect that community-based cervical cancer screening will reach a substantially larger portion of eligible women than clinic-based testing. Our findings will help guide implementation and optimization of a community-based HPV testing model. While we anticipate that the community-driven enhanced intervention will be more effective at linking women to facilities for treatment than the standard referral system, this study will allow us to test both models and look at various aspects of implementation, including cost-effectiveness. In addition to these findings, we will provide a model for a successful strategy to link women to treatment within cervical cancer screening program and to provide program leaders and policymakers with a tool kit to design and evaluate a context-specific enhanced linkage strategy that could be implemented in their own settings. We expect that community-based HPV screening will have a greater cost effectiveness and public health impact than clinic-based testing, and that enhanced linkage strategies will amplify these differences. Overall, our findings will provide evidence to inform clinical protocols and government policy regarding the provision of cervical cancer prevention strategies and provide a guide for adaptation and evaluation of similar programs in other settings. Ultimately programs that both use evidence-based techniques and reach a large proportion of the population will impact the millions of women at risk for cervical cancer in low resource countries worldwide.

Conclusions

This project will have broad implications at both local and national policy and planning levels, given the enthusiasm of the Kenya Ministry of Health and Division of Reproductive Health to implement national cervical cancer prevention strategies and their partnership in this project. When the analyses are complete, we will have produced a comprehensive description of barriers and facilitators to providing clinic and community-based cervical cancer screening through HPV testing, determined which strategy has greater reach and a better cost-effectiveness profile, and developed a strategy to improve linkage to treatment in partnership with the community. If a community-based screening strategy is shown to have more reach with a favorable cost-effectiveness profile, this could be a viable strategy for roll-out in similar settings in Kenya and possibly for adaptation to other East African countries with a high cervical cancer burdens. Just as importantly, if community-based testing is more effective and scalable than clinic-based testing, we will explore factors necessary to improve access to clinic for cervical cancer screening and other preventive care services.

Additional file

Additional file 1: WHO Trial Registry Data. (PDF 86 kb)

Abbreviations

CHC: Community health campaign; CIN: Cervical intraepithelial neoplasia; DALY: Disability adjusted life year; FGD: Focus group discussion; HPV: Human papillomavirus; ICER: Incremental cost-effectiveness ratio; LEEP: Loop electrosurgical excision procedure; RE-AIM: Reach, effectiveness, adoption, implementation and maintenance (Implementation Framework); WHO: World health organization

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Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Authors' contributions

MJH conceived the study, led the study design, wrote the protocol and is the overall study PI. RH provided assistance with the conceptualization of the Implementation Framework. JK led the costing and cost-effectiveness analysis design. JS assisted with the HPV testing component of the study. EB and CRC assisted with the writing and contextualization of the study design to the local environment and EB acts as the site PI. All authors have read and approved the final version of the protocol.

Ethics approval and consent to participate

The KEMRI Scientific and Ethics Review Unit (SERU; #2918), the Duke University Institutional Review Board (Pro0007742) and and the University of California San Francisco (UCSF) Human Research Protection Program Institutional Review Board (14–13,698) reviewed and approved the study. All participants gave their written informed consent to participate in the study prior to data or specimen collection.

Consent for publication

Not Applicable

Competing interests

The authors declare that they have no competing interests.

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Reporting checklist for qualitative study.

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		Reporting Item	Page Number
	#1	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	1
	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	2
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	4, 5
Purpose or research question	#4	Purpose of the study and specific objectives or questions	5
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The	6

		rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
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Context	#7	Setting / site and salient contextual factors; rationale	5
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	5
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	7
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	6
Data collection instruments and technologies	#11	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	6
Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	7
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	6
Data analysis	#14	Process by which inferences, themes, etc. were identified and	6

		developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	6
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	7-13
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	7-13
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	13
Limitations	#19	Trustworthiness and limitations of findings	15
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	17
Funding	#21	Sources of funding and other support; role of funders in data collection, interpretation and reporting	17

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BMJ Open

"I'm here to save my life:" a qualitative study of experiences navigating a cryotherapy referral system for human papillomavirus-positive women in western Kenya

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"I'm here to save my life:" a qualitative study of experiences navigating a cryotherapy referral system for human papillomavirus-positive women in western Kenya

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Abstract

Background: We sought to understand the beliefs, social norms and logistical factors that affect HPV-positive women's uptake of cryotherapy treatment as part of a two-part cervical cancer screening strategy in rural Kenya.

Methods: In-depth interviews within a parent cluster-randomized trial

Setting: Government-run county hospital in western Kenya.

Participants: 273 of 372 (73.4%) HPV-positive women who underwent cryotherapy

Results: Many women feared that an HPV infection meant they would develop cancer. Almost all women reported initial fear of the treatment procedure, followed by a more positive experience than anticipated. Lacking funds for transportation to the treatment site was the most common barrier. Women felt that decentralized treatment would be the most important facilitator of greater access. Spousal encouragement and financial support were key facilitators of treatment access, however many women felt that other husbands in the community would not be supportive. Women described successfully acquiring treatment as empowering, and almost all would recommend seeking cryotherapy to other women who test HPV positive. Most felt eager to share their own experiences with others to encourage treatment.

Conclusions: The main facilitators of treatment access were understanding of the health risks and sense of empowerment. A decentralized treatment model or transportation support may facilitate access, along with improved health messaging about HPV infection, cancer, and the treatment process. Focusing on women's personal feelings of empowerment may further improve uptake and satisfaction. This data will be used to design a strategy to improve linkage to treatment.

Trial Registration: NCT02124252

Article Summary

Strengths and Limitations of the study

- This study provides insight into women’s experience obtaining cryotherapy after a receiving positive HPV test result in western Kenya.
- The perspectives provided will allow for improved contextualization of cervical cancer prevention programs in similar settings.
- These qualitative findings are exploratory, and may not be reflective of larger patterns or associations.
- Women were interviewed by trained study staff, so there may have been social desirability bias.
- We did not interview women who were lost-to-follow-up, and may have therefore have had even more barriers than those identified in this study

Introduction:

Cervical cancer, despite being one of the most preventable cancers through vaccination and screening, remains the fourth most common cancer among women worldwide.[1] Now rare in wealthier countries due to the success of cytology-based prevention programs, cervical cancer continues to be a major public health issue in low and middle-income countries (LMICs). Effective population-based screening, coupled with linkage to treatment for screen-positive women, is critical to preventing the development of cervical cancer. In Kenya, where screening rates range between 3 and 14%, cervical cancer is the second most common cancer in women, and the leading cause of cancer related mortality.[2]

Strategies to address the lack of screening programs in LMICs include simpler screening techniques coupled with cryotherapy for women who screen positive. Cryotherapy is relatively inexpensive, can be performed by non-physician providers and does not require electricity. It has been promoted along with Visual Inspection with Acetic Acid (VIA) as a part of a same day "see & treat" strategy, although the expense and logistical challenges of maintaining supplies, space, and personnel for cryotherapy in remote settings make single visit strategies impossible in most settings.[3, 4]

Another simple screening technique is low-cost human papillomavirus (HPV) testing.[5, 6] The World Health Organization incorporated the growing body of evidence supporting HPV testing into recommendations for screening programs in low resource settings.[7] The current guidelines include HPV primary screening as the preferred modality, followed by cryotherapy. As HPV testing has become more widely available and the evidence for its use more convincing, programs are starting to move from "see & treat" to "screen & treat," referring women for treatment based on a positive HPV result. While this may be more effective at decreasing cervical precancer and cancer, there are no currently available HPV tests that allow for same-visit results. Therefore, programs must take into consideration how to deliver HPV test results and counseling in a way that fosters understanding and facilitates women's uptake of the appropriate follow-up. An effective HPV-based screening program must take into account the multitude of sociocultural factors such as stigma, fear, and misperceptions, along with the logistical and health systems factors that affect a woman's decision-making and ability to seek screening, understand her results and obtain treatment if needed.

While multiple studies have evaluated effective screening methods for women in western Kenya, there remains a gap in understanding effective strategies to link women who screen positive for HPV to appropriate follow-up and treatment.[8-12] Given that HPV-based strategies are relatively new to LMICs, there is very little qualitative data exploring women's experience with treatment. Understanding the knowledge, beliefs, social norms, and logistical factors that affect women's decision and ability to seek treatment are essential in the design of effective context-specific treatment strategies. We used the Consolidated Framework for Implementation Research (CFIR) to explore the contextual factors that may have facilitated HPV-positive women's access to appropriate treatment within a community-based screening program. [13]

Materials and Methods:

Study Design

We utilized qualitative data to explore the barriers and facilitators of treatment access for women who tested HPV positive as part of a two-phase cluster randomized trial in rural western Kenya.[14] In the first phase, 12 communities in Migori County were randomized to screening using self-collected HPV tests either through community health campaigns (CHCs) or in health facilities. In both the CHC and health facility arms, women who tested HPV positive were notified of their results and referred to the Migori County Hospital for treatment with cryotherapy. After treatment, women were invited to participant in an in-depth-interview (IDI) regarding their experience.

The distance between Migori County Hospital and the 12 study communities ranged from 11 to 94 kilometers. Transport around the county was available via motorcycles, public buses and private taxis. In the hospital compound, treatment was provided by nurses who had undergone additional training in both cryotherapy and study procedures prior to study initiation. The medical superintendent and an experienced nurse facilitator provided supervision as needed.

Women underwent VIA prior to treatment, followed by cryotherapy unless the cervical anatomy was abnormal, the lesion was too large for the probe, or there was suspicion for cancer. In the first two cases, the woman would be referred for LEEP within the same hospital. If there was suspicion for cancer, she was offered a biopsy and referred for management of cancer. All costs associated with cryotherapy or LEEP were covered by the study. Women did not receive compensation for transport or monetary incentives for participation in the study.

Data Sources

IDI guides were developed using selected CFIR constructs to elicit responses about the client-sided experience and perceptions of treatment (Table 1). Selected constructs included adaptability, patient needs and resources and complexity of proposed intervention methods. IDI guides were developed in English and translated and conducted in the most common local languages (Dholuo and Kiswahili) by researchers fluent in those languages. The first part of the IDIs consisted of closed-ended questions about sociodemographic characteristics, sexual behavior, gynecological history, HIV status, cervical cancer screening, and HPV. Interviewers entered this data directly into Open Data Kit installed onto study tablets. The second part of the interviews consisted of open-ended questions that probed women on what they understood about HPV and treatment for HPV, their feelings and experience with treatment, barriers and facilitators to treatment, stigma and desire for privacy, and male and community leader roles in facilitating cervical cancer prevention. Interviews lasted between 15 and 25 minutes. This data was recorded on the tablets, and then transcribed and translated. All translations were reviewed with the audio by the study coordinator for accuracy.

Data Analysis

Using thematic analysis, one member of the research team created the codebook using the IDI guide for structure and four sample interviews to identify additional themes. The codebook was then reviewed and revised by the entire team, followed by a round in which all four researchers sample coded ten interviews to test and revise the codebook. All analysis and codebook development was done using NVivo 11™ software (QSR International, London, United

Table 1: Refined CFIR constructs and key findings regarding HPV-positive women's experiences with a referral-based cryotherapy treatment strategy

Construct	Topics Covered	Key Findings
Intervention Characteristics		
Relative Advantage	• What are the advantages of the proposed treatment model?	• Offered free of charge, outpatient
Adaptability	• What are other models of treatment that would facilitate increased access? • What are factors of the current treatment model that could be improved?	• Decentralized treatment or transportation support would improve the model
Complexity	• Perceptions of treatment feasibility and sustainability • What is the participant's understanding of the screening and treatment cascade?	• Women had unanswered questions after treatment, regarding follow-up, need for medication or potential impact on fertility
Outer Setting		
Patient Needs and Resources	• What can the health facilities do to facilitate patient treatment acquisition?	• Provider respect was high
Inner Setting		
Culture	• What is the level and impact of male support? • How could community leader involvement facilitate treatment?	• Male financial and moral support were important to treatment acquisition • Many were concerned about post-treatment abstinence or re-infection • Ambivalence about community leader involvement
Access to Knowledge & Information	• How can outreach and education strategies be improved? • How does peer education and support impact treatment acquisition?	• Peer education noted in both educating about screening and encouraging treatment
Characteristics of Individuals		
Knowledge & Beliefs about the Intervention	• Did women understand the meaning of a positive HPV result? • Did women understand the process and availability of treatment? • Do women understand the importance of treatment for their health?	• Role of HPV in development of cancer was well understood, however some women equated an HPV positive result with cancer • Women knew that early treatment would be simpler than treatment for advanced disease
Self-efficacy	• Do women prioritize accessing treatment for their health? • How do health beliefs and self-efficacy impact women's ability to overcome barriers to treatment?	• Women felt knowing HPV status allowed them to move on a health action (treatment) • Treatment had an empowering influence • Post-treatment, women felt that they could/should be role models
Individual Stage of Change	• What role do peer networks or social support play in treatment access? • What role do individual health beliefs play in reactions or decisions about treatment for a positive HPV test?	• Women felt relief at knowing HPV status • Fear surrounding HPV result and association with cancer led to some inaction

Kingdom). The team then met to discuss and make final revisions to the codebook. All interviews were coded twice by two separate members of the research team. Coding reports were then reviewed collaboratively to identify important themes and finalize mapping onto the modified CFIR framework.

Patient and Public Involvement

The research question and measures were informed by preliminary work done in partnership with the Ministry of Health to evaluate barriers and facilitators of cervical cancer screening and treatment. We also carried out focus group discussions with women living in Migori to plan and implement Phase 1 of the study (manuscript submitted). Patients were not involved in recruitment, as all women undergoing treatment were asked by a research assistant to participate in an interview. Results have already been disseminated to the participants through two key stakeholder meetings. In addition, selected participants were invited to participate in a working group to amend the treatment implementation strategy for Phase 2.

Results:

Between February and December 2016, 5898 women underwent cervical cancer screening in both CHC and health facilities and 1043 (17.4%) tested positive for HPV. Out of these women, 399 (38.3%) women presented for treatment at Migori County Hospital and 372 (35.6%) underwent cryotherapy. Three women were referred for LEEP and one for invasive cancer management. Among the 372 treated HPV-positive women, 273 women (73.4%) completed an in-depth interview after their treatment. There was no difference in the clinical or demographic characteristics in the participants from the original study arm, or between those who agreed to an interview and those who declined. Women traveled a mean of 37 kilometers to get to Migori for treatment, and almost all used a paid form of transportation (bus, taxi or motorbike).

Knowledge and perceptions of HPV positivity and treatment value

Many women expressed confidence in their level of knowledge about the relationship between HPV and cervical cancer, and the role of treatment in protecting their health. Specifically, many understood that the recommended treatment was simpler and more effective than it would be if HPV developed into cervical cancer.

> *"I learnt that, having HPV doesn't mean you have the disease, it is just a sign that it may develop in to a disease and when you have the virus and it is detected early enough it can be treated"*

Although many women were able to make fact-based statements about HPV, and professed confidence in their knowledge, some expressed fear, anxiety and misperceptions about their positive HPV results and the association with cancer. This was reflected in women's feelings around the time they received their results and their concern that the treatment would not "cure" their cancer.

> *"I felt pain at heart, since I do hear that those with cancer do not survive, even now I still have no assurance of good health."*

Though some women reported worry or anxiety about their test result, many felt relief that they were now aware of their HPV status and could get treatment.

> *"What came into my mind after I was confirmed HPV positive was just on how I can access treatment my focus now is how I can be on treatment and that is my key challenge as at now."*

<u>Treatment Experience</u>

Women were almost uniformly positive about provider respect, privacy, adequate explanation, and ability to ask and have their questions answered. Most women also reported minimal pain or cramping, with no reported complications with the procedure. Overall, women expressed relief that the procedure was not as difficult as they had feared, with responses similar to the comment below.

> *"When I came from home, people were saying that this treatment is painful but I have not felt any pain. I have found it to be good and the pain that people are talking about is not there."*

When asked how to improve the treatment experience, women had limited suggestions, or focused on access issues. This may not reflect satisfaction with the treatment model as much as a feeling that it was the role of "health care providers or "doctors" to "improve the experience". *"It is you as healthcare providers to find on ways of making it more comfortable."*

Unanswered Questions

Despite reporting adequate explanation and overall treatment satisfaction, a number of unanswered questions or misperceptions regarding cervical cancer or follow-up arose throughout the interviews. When asked whether women had unanswered questions at the end of the screening/notification and treatment process, they revealed underlying fears about extent of disease/outcomes of treatment (future fertility, death from cancer, etc). Many women were under the impression that they would be given drugs to treat HPV, like treatment for malaria or HIV management. *"I have learnt that in case I will be given drugs then I will have to take them to help prevent the virus from advancing into cervical cancer."* Women who mentioned drugs recounted that they were *told* they would be given drugs, although this was not an intended part of the health messaging during screening or treatment.

Some women believed that if they were infected with HPV, they would not be able to give birth, or they should not get pregnant because the fetus would be infected with HPV. Related to the fear of infertility, women reported believing that family planning methods caused their positive HPV result or would cause cervical cancer.*"I thought that I had cervical cancer because since I went for family planning [IUCD]. I have not been feeling okay in the uterus."*

Identifying Specific Barriers and Facilitators to Treatment Access

When women were asked whether they encountered any barriers or difficulty accessing treatment, and most answered no. However, when prompted, many confirmed that they had to miss work, struggled to find childcare or transportation funds, or traveled a long distance. Some women expressed the belief that if a woman is sick or valued her health, there were no barriers that could stop her from accessing treatment in statements like the following: *"It can only be far for someone who is not sick but if you are sick, you cannot say that it is far. I'm here to save my life."*

Lack of access to means of transportation and/or funds to hire transport were the main barriers that resulted in delays in treatment. Women also worried about future transport costs if the disease progressed, explicitly stating that they anticipated missing future appointments.

> *"I do not know what to tell you. If you have money you can access everywhere, but if you do not you cannot make it on foot. The poor will die of even diseases that can be treated unlike the rich."*

When asked about how to make treatment access easier, many women mentioned that telling their own story of treatment to women who tested positive for HPV would be helpful, suggesting that peer education and social support may play a large role in decision to get treated. Women wanted to publicize that treatment was free, easy, quick and important for women's long-term health. Examples of these sentiments include the following:

> *"When the [positive] results came I was surprised. I then took time and went to my friends who also were HPV positive and shared with them, we encouraged each other and set dates for coming for treatment."*

> *"I would tell her it is important for her to know her HPV status because she would be able to know if she is at a high risk of developing cervical cancer…Treatment is good. It is free and very easy. There is no pain, so it is good. That is how I would encourage her."*

Women suggested two changes in the treatment model that could facilitate treatment for women in the community, (1) a decentralized treatment model that provides treatment in more rural health facilities, closer to homes, or a mobile treatment unit that moves periodically through communities and (2) transportation provisions or reimbursements, echoing the main barrier to treatment access.

Finally, a substantial number of women felt that greater awareness of or access to *screening* would increase uptake of treatment. Women suggested repeating screening in the communities for those who had missed earlier campaigns and increasing involvement of lay health workers, or community health volunteers, in outreach and education around screening.

Support from Peer Networks and Community Leaders

Women wanted to share their diagnosis with others in their community, both to be able to obtain psychological and financial support for treatment and to set an example. Most reported that privacy around their HPV status was not important to them.

> *"I am comfortable with any other person knowing my status because, he or she might be able to support me if am sick or I might be able to encourage and support a person who is sick but is too scared to receive treatment."*

A small minority of women who did not want to share their diagnosis with others, apart from their spouse or co-wives, gave reasons including a general desire for privacy about their own health, without specific mention of HPV or cervical cancer related stigma.

> *"The reason why I did not want anyone else to know is because some people tend to exaggerate things, if one hears you have this disease, they may start telling you how you have a very bad disease and that you will die soon"*

Women held contradictory opinions regarding the role of community leaders in facilitating treatment. Women who were in favor stated that leaders could "*mobilize women to seek treatment", while those opposed feared a loss of privacy, stating that "community leaders would spread rumors to the community members."*

Male Partner Involvement

Male partner involvement emerged around treatment access, post-treatment care and fears of reinfection from their partners.

Almost all women interviewed said the decision to seek treatment was theirs alone. However, they did feel like male support or opposition played a role in access of treatment services. Interestingly, most women stated that while men in general would likely not be supportive of their wives obtaining treatment, their own spouse had been. Reasons for other husbands' perceived lack of support were related to a lack of understanding or belief that HPV is a real threat, and low prioritization of their wives' health. Male support was generally described as financial support for transportation, with a minority naming encouragement or moral support for treatment. Women's comments indicate either a perception about lack of male support for other women in the community, while descriptions of their own experience suggest that male support was a key factor in their ability to obtain treatment (as all the women in this group had successfully obtained treatment).

> *"My husband support[ed] screening so that should I be confirmed positive, I start the treatment in time before it worsens…he provided me with fare and asked me to leave early so I can get to the hospital in time.*

> *"Some do not understand cervical cancer and some just care less about their wives and cervical cancer hence not becoming supportive. Other men are supportive when they value the lives of their female partners."*

Standard counseling after cryotherapy includes abstinence for a month, and use of a condom after resumption of sexual activity for six months to prevent spread of HPV or reinfection. A few women expressed concern about cultural and social beliefs regarding sexual activity that would prevent their husbands from supporting them through the recovery period, or use of a condom afterwards. Some women even requested that a health provider speak with their husband.

> *"I had a concern with the issue of not having sexual contact with my husband for a month. We built a new house, which we are supposed to enter into in the course of this week. As Luos, we have our customs that we must uphold, what will I do?"*

Concerns about the ability to be abstinent following treatment were echoed in some women's thoughts about the futility of treatment in situations where they perceived little control over possible reinfection. Concerns were raised about safe relations with their husband, inability to negotiate condoms and concerns about [re]infection among co-wives.

> *"It is said that men are the one who infects us, and us still being a young couple we are bound to have sexual relations, what can be done so to men so that they do not spread the disease?"*

> *"Supposing I have a co-wife, how will I know that she has also been treated so that we can all be free and not use condoms?"*

Treatment and Empowerment

Although this group of women who were able to overcome barriers and access treatment for their HPV likely had higher baseline levels of empowerment than women who did not get treatment, any women expressed a sense of personal empowerment from the process of either undergoing treatment or from gaining an understanding of the impact of HPV on their health. This may have played as a key factor in overcoming barriers to treatment.

> *"I have come to seek treatment for a better future; I want a future so that I can continue taking care of [my children]"*

Finally, almost all women said they would recommend treatment to other women who they knew tested HPV positive, stating that the treatment was easier than they thought, free, quick and almost painless. Importantly, many felt that they had an important role to play as peer educators or advocates to convince other women who tested HPV positive to get treatment. Often, women expressed that their treatment experience changed their minds about privacy and the importance of sharing their experience.

> *"I never felt like letting anyone know about my treatment, now that I have, I can easily encourage my neighbor to seek for treatment in case she's positive."*

> *"I would tell her my experience about the treatment. How easy and how painless it is. How the doctors are prepared and how they talk nicely to us. I would tell her she has nothing to fear and she should gather courage and come."*

Discussion:

Appropriate follow-up for HPV-positive women is a critical component in cervical cancer prevention and control; the success of programs in LMICs is often limited by attrition between screening and treatment. This study used the CFIR framework to explore the contextual factors surrounding women's uptake of treatment after a positive HPV test in rural Kenya. We found that women were generally satisfied and even empowered by their treatment experience. The results also showed that the belief that the treatment they were seeking would have an important and positive impact on their health enabled women to overcome the barriers of fear, lack of transportation funds and distance to the treatment center.

These findings add substantially to a body of work that has primarily focused on structural, financial, and policy-related barriers and facilitators to the implementation of cervical cancer screening and treatment programs by exploring the patient experience from receiving results to navigating treatment access.[15, 16] The participant perspectives provide important insight into ways the treatment model can be improved. To our knowledge, this is the only study to assess patient-level factors impacting cryotherapy treatment in a low-resource setting using the CFIR framework. The use of a standardized framework is important to developing a sustainable and effective enhanced linkage to treatment strategy with the potential for replication in other settings.

The fact that empowerment associated with treatment emerged so strongly was encouraging and indicated a facilitating culture. However, substantial logistical and financial barriers remain in place for women in this model, despite free screening and treatment. Women traveled an average distance of over thirty kilometers and almost all women required some form of hired transportation. While the majority of women did not recall income loss, or reported a loss of less than 1000 Kenya Shillings ($10 US), the cost of transportation represented a significant burden, even among this group of women who were not lost-to-follow-up. Partner support was significant, and most often appeared in the form of payment for transportation. While almost all women stated that the decision to seek treatment was their own, their reliance on partners for financial support was crucial and may have important implications for future cervical cancer prevention and treatment initiatives. The role of partner support needs to be explored among women who were not able to obtain treatment. The frequency at which the costs of transportation to a distant treatment site and the reliance on partners were reported indicates a need to explore the decentralization of treatment with or without a mobile treatment unit, the use of transportation vouchers, or assistance of some type that emphasized transportation.

The use of peer educators to help encourage and facilitate treatment access may also be a strategy to overcome the logistical hurdles using an empowerment framework. While other studies have not shown educational interventions to be as effective as other implementation strategies for cervical cancer prevention,[17] peer-led counseling has increased perceptions of screening benefits and engagement in screening activities.[18, 19] Peer-to-peer education has played a large role in the success of HIV programs in this region, so participants were likely to have experience and comfort with this. Importantly, women saw themselves as potential peer educators, using their positive experiences with treatment to convince other women to get treated. In this way, the self-efficacy they displayed in obtaining treatment would be transformed into a sense of personal empowerment through a reflection of their own success and influence on others.

This qualitative data clearly elucidated points of clarification for the educational counseling provided throughout the outreach, screening and treatment activities. Although the current education modules stress that HPV is not cancer, some women continued to believe that a positive HPV result was synonymous with having cancer, which then caused cancer-related fear, sometimes resulting in inaction. Educational content and the mechanisms by which women are notified of their results should be rigorously tested to ensure clarity, as fear of cancer or more invasive procedures may prevent women from seeking appropriate treatment. In addition, these data highlight a need to address the misconceptions about family planning, infertility, and the need for medication as part of treatment both during outreach and at the time of screening and treatment. The persistent expectation that treatment would involve long-term medications may reflect an interpretation of medication as synonymous with treatment, as is the case with the more common diseases in the area: HIV, TB, and malaria. Based on these findings we updated the educational material to include more precise descriptions of the cryotherapy procedure and clarify that treatment does not require medication.

While this data highlighted crucial information that allows us to further understand how and why women are able to access treatment when free treatment is offered, there are limitations inherent to the study design. The current study is missing the voices and experience of women who were unable to access treatment, who were the majority of women screened. For example, in this population of women who had successfully accessed treatment, almost all were in a relationship or married, which was possibly a key factor in their success with navigating treatment. While the qualitative data suggests partner financial support was key in reaching treatment sites, we must identify and work with women who were lost-to-follow-up to fully begin to understand and address insurmountable barriers. In addition, as these interviews were done by the study team in proximity to treatment sites, there may have been some social desirability bias in responses related to treatment experience and provider respect.

Conclusions

These data provide valuable insight on the implementation of a community-based cervical cancer screening program through the perspectives of HPV-positive women who were able to access free treatment through referral to a county government hospital. While many women reported feelings of self-efficacy and empowerment, and were pleased with their experience deciding and accessing treatment, they represent the minority of patients. Despite multiple efforts to counsel women about the importance and availability of treatment, over half of the women who tested HPV-positive in the parent study did not access treatment. We have identified specific barriers and potential facilitators to treatment access that will inform new implementation strategies and ways to intensify efforts to reach the wider population of women who were lost-to-follow-up and work with health care teams to develop a linkage to treatment strategy that ensures greater follow-up with appropriate care.

List of abbreviations:

CFIR: Consolidated Framework for Implementation Research

HIV: Human Immunodeficiency Virus

HPV: Human papillomavirus

IDI: In-depth Interview

TB: tuberculosis

WHO: World Health organization

Declarations:

Ethics approval and consent to participate:
The KEMRI Scientific and Ethics Review Unit (SERU; #2918), the Duke University Institutional Review Board (Pro0007742) and and the University of California San Francisco (UCSF) Human Research Protection Program Institutional Review Board (14-13698) reviewed and approved the study. All participants gave their written informed consent to participate in the study prior to data or specimen collection.

Consent for publication:
Not Applicable

Availability of Data and Materials:
Deidentified participant data and coding reports are available at request from Dr. Huchko (ORCID # 0000-0002-4081-4768) for up to ten years with permission of the Duke and KEMRI ethical review committees.

Competing Interests:
The authors declare that they have no competing interests

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Authors' contributions:
MJH is the overall study PI. She conceived the study, led the study design, led the coding and analysis, and wrote the manuscript. KA, SY and SI assisted with the coding, analysis and conceptual framework. SY lead data collection activities. SI led data management. EB assisted with the manuscript preparation and acts as the site PI. All authors have read, actively edited and approved the final version of the protocol.

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Reporting checklist for qualitative study.

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		Reporting Item	Page Number
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	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	2
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	4, 5
Purpose or research question	#4	Purpose of the study and specific objectives or questions	5
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The	6

		rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	6
Context	#7	Setting / site and salient contextual factors; rationale	5
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	5
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	7
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	6
Data collection instruments and technologies	#11	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	6
Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	7
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	6
Data analysis	#14	Process by which inferences, themes, etc. were identified and	6

		developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	6
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	7-13
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	7-13
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	13
Limitations	#19	Trustworthiness and limitations of findings	15
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	17
Funding	#21	Sources of funding and other support; role of funders in data collection, interpretation and reporting	17

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“I’m here to save my life:” a qualitative study of experiences navigating a cryotherapy referral system for human papillomavirus-positive women in western Kenya

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“I’m here to save my life:” a qualitative study of experiences navigating a cryotherapy referral system for human papillomavirus-positive women in western Kenya

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Abstract

Background: We sought to understand the beliefs, social norms and logistical factors that affect HPV-positive women's uptake of cryotherapy treatment as part of a two-part cervical cancer screening strategy in rural Kenya.

Methods: In-depth interviews within a parent cluster-randomized trial

Setting: Government-run county hospital in western Kenya.

Participants: 273 of 372 (73.4%) HPV-positive women who underwent cryotherapy

Results: Many women feared that an HPV infection meant they would develop cancer. Almost all women reported initial fear of the treatment procedure, followed by a more positive experience than anticipated. Lacking funds for transportation to the treatment site was the most common barrier. Women felt that decentralized treatment would be the most important facilitator of greater access. Spousal encouragement and financial support were key facilitators of treatment access, however many women felt that other husbands in the community would not be supportive. Women described successfully acquiring treatment as empowering, and almost all would recommend seeking cryotherapy to other women who test HPV positive. Most felt eager to share their own experiences with others to encourage treatment.

Conclusions: The main facilitators of treatment access were understanding of the health risks and sense of empowerment. A decentralized treatment model or transportation support may facilitate access, along with improved health messaging about HPV infection, cancer, and the treatment process. Focusing on women's personal feelings of empowerment may further improve uptake and satisfaction. This data will be used to design a strategy to improve linkage to treatment.

Trial Registration: NCT02124252

Article Summary

Strengths and Limitations of the study

- This study provides insight into women’s experience obtaining cryotherapy after a receiving positive HPV test result in western Kenya.
- The perspectives provided will allow for improved contextualization of cervical cancer prevention programs in similar settings.
- These qualitative findings are exploratory, and may not be reflective of larger patterns or associations.
- Women were interviewed by trained study staff, so there may have been social desirability bias.
- We did not interview women who were lost-to-follow-up, and may have therefore have had even more barriers than those identified in this study

Introduction:

Cervical cancer, despite being one of the most preventable cancers through vaccination and screening, remains the fourth most common cancer among women worldwide.[1] Now rare in wealthier countries due to the success of cytology-based prevention programs, cervical cancer continues to be a major public health issue in low and middle-income countries (LMICs). Effective population-based screening, coupled with linkage to treatment for screen-positive women, is critical to preventing the development of cervical cancer. In Kenya, where screening rates range between 3 and 14%, and vaccination for human papillomavirus (HPV) is not yet available, cervical cancer is the second most common cancer in women, and the leading cause of cancer related mortality.[2]

Strategies to address the lack of screening programs in LMICs include simpler screening techniques coupled with cryotherapy for women who screen positive. Cryotherapy is relatively inexpensive, can be performed by non-physician providers and does not require electricity. It has been promoted along with Visual Inspection with Acetic Acid (VIA) as a part of a same day “see & treat” strategy, although the expense and logistical challenges of maintaining supplies, space, and personnel for cryotherapy in remote settings make single visit strategies impossible in most settings.[3, 4]

Another simple screening technique is low-cost HPV testing.[5, 6] The World Health Organization incorporated the growing body of evidence supporting HPV testing into recommendations for screening programs in low resource settings.[7] The current guidelines include HPV primary screening as the preferred modality, followed by cryotherapy. As HPV testing has become more widely available and the evidence for its use more convincing, programs are starting to move from “see & treat” to “screen & treat,” referring women for treatment based on a positive HPV result. While this may be more effective at decreasing cervical precancer and cancer, there are no currently available HPV tests that allow for same-visit results. Therefore, programs must take into consideration how to deliver HPV test results and counseling in a way that fosters understanding and facilitates women’s uptake of the appropriate follow-up. An effective HPV-based screening program must take into account the multitude of sociocultural factors such as stigma, fear, and misperceptions, along with the logistical and health systems factors that affect a woman's decision-making and ability to seek screening, understand her results and obtain treatment if needed.

While multiple studies have evaluated effective screening methods for women in western Kenya, there remains a gap in understanding effective strategies to link women who screen positive for HPV to appropriate follow-up and treatment.[8-12] Given that HPV-based strategies are relatively new to LMICs, there is very little qualitative data exploring women's experience with treatment. Understanding the knowledge, beliefs, social norms, and logistical factors that affect women's decision and ability to seek treatment are essential in the design of effective context-specific treatment strategies. We used the Consolidated Framework for Implementation Research (CFIR) to explore the contextual factors that may have facilitated HPV-positive women's access to appropriate treatment within a community-based screening program. [13]

Materials and Methods:

Study Design

We utilized qualitative data to explore the barriers and facilitators of treatment access for women who tested HPV positive as part of a two-phase cluster randomized trial in rural western Kenya.[14] In the first phase, 12 communities in Migori County were randomized to screening using self-collected HPV tests either through community health campaigns in central locations in the villages (CHCs) or in health facilities. In both the CHC and health facility arms, education and outreach was led by community health volunteers, and women who tested HPV positive were notified of their results and referred to the Migori County Hospital for treatment with cryotherapy.[15] After treatment, women were invited to participant in an in-depth-interview (IDI) regarding their experience.

The distance between Migori County Hospital and the 12 study communities ranged from 11 to 94 kilometers. Transport around the county was available via motorcycles, public buses and private taxis. In the hospital compound, treatment was provided by nurses who had undergone additional training in both cryotherapy and study procedures prior to study initiation. The medical superintendent and an experienced nurse facilitator provided supervision as needed. Women underwent VIA prior to treatment, followed by cryotherapy unless the cervical anatomy was abnormal, the lesion was too large for the probe, or there was suspicion for cancer. In the first two cases, the woman would be referred for an loop electrosurgical excision procedure (LEEP) within the same hospital. If there was suspicion for cancer, she was offered a biopsy and referred for management of cancer. All costs associated with cryotherapy or LEEP were covered by the study. Women did not receive compensation for transport or monetary incentives for participation in the study.

Data Sources

IDI guides were developed using selected CFIR constructs to elicit responses about the client-sided experience and perceptions of treatment (Table 1). Selected constructs included adaptability, patient needs and resources and complexity of proposed intervention methods. IDI guides were developed in English and translated and conducted in the most common local languages (Dholuo and Kiswahili) by researchers fluent in those languages. The first part of the IDIs consisted of closed-ended questions about sociodemographic characteristics, sexual behavior, gynecological history, HIV status, cervical cancer screening, and HPV. Interviewers entered this data directly into Open Data Kit installed onto study tablets. The second part of the interviews consisted of open-ended questions that probed women on what they understood about HPV and treatment for HPV, their feelings and experience with treatment, barriers and facilitators to treatment, stigma and desire for privacy, and male and community leader roles in facilitating cervical cancer prevention. Interviews lasted between 15 and 25 minutes. This data was recorded on the tablets, and then transcribed and translated. All translations were reviewed with the audio by the study coordinator for accuracy.

Data Analysis

Using thematic analysis, one member of the research team created the codebook using both the IDI guide for structure and four sample interviews to identify additional themes that together facilitated a more nuanced interpretation of the data .[16] The codebook was then reviewed and revised by the entire team, followed by a round in which all four researchers sample coded ten interviews to test and revise the codebook. All analysis and codebook development was done using NVivo 11™ software (QSR International, London, United

Table 1: Refined CFIR constructs and key findings regarding HPV-positive women's experiences with a referral-based cryotherapy treatment strategy		
Construct	**Topics Covered**	**Key Findings**
Intervention Characteristics		
Relative Advantage	• What are the advantages of the proposed treatment model?	• Offered free of charge, outpatient
Adaptability	• What are other models of treatment that would facilitate increased access? • What are factors of the current treatment model that could be improved?	• Decentralized treatment or transportation support would improve the model
Complexity	• Perceptions of treatment feasibility and sustainability • What is the participant's understanding of the screening and treatment cascade?	• Women had unanswered questions after treatment, regarding follow-up, need for medication or potential impact on fertility
Outer Setting		
Patient Needs and Resources	• What can the health facilities do to facilitate patient treatment acquisition?	• Provider respect was high
Inner Setting		
Culture	• What is the level and impact of male support? • How could community leader involvement facilitate treatment?	• Male financial and moral support were important to treatment acquisition • Many were concerned about post-treatment abstinence or re-infection • Ambivalence about community leader involvement
Access to Knowledge & Information	• How can outreach and education strategies be improved? • How does peer education and support impact treatment acquisition?	• Peer education noted in both educating about screening and encouraging treatment
Characteristics of Individuals		
Knowledge & Beliefs about the Intervention	• Did women understand the meaning of a positive HPV result? • Did women understand the process and availability of treatment? • Do women understand the importance of treatment for their health?	• Role of HPV in development of cancer was well understood, however some women equated an HPV positive result with cancer • Women knew that early treatment would be simpler than treatment for advanced disease
Self-efficacy	• Do women prioritize accessing treatment for their health? • How do health beliefs and self-efficacy impact women's ability to overcome barriers to treatment?	• Women felt knowing HPV status allowed them to move on a health action (treatment) • Treatment had an empowering influence • Post-treatment, women felt that they could/should be role models
Individual Stage of Change	• What role do peer networks or social support play in treatment access? • What role do individual health beliefs play in reactions or decisions about treatment for a positive HPV test?	• Women felt relief at knowing HPV status • Fear surrounding HPV result and association with cancer led to some inaction

Kingdom). The team then met to discuss and make final revisions to the codebook. All interviews were coded twice by two separate members of the research team. Coding reports were then reviewed collaboratively to identify important themes and finalize mapping onto the modified CFIR framework.

Patient and Public Involvement

The research question and measures were informed by preliminary work done in partnership with the Ministry of Health to evaluate barriers and facilitators of cervical cancer screening and treatment. Prior to study implementation, we also carried out focus group discussions with women living in Migori to plan and implement Phase 1 of the study (manuscript submitted). For this study, patients were not involved in identification or recruitment or participants, as all women undergoing treatment were asked by a research assistant to participate in an interview after their treatment had been completed. Results have already been disseminated to the participants through two key stakeholder meetings. In addition, selected participants were invited to participate in a working group to amend the treatment implementation strategy for Phase 2.

This protocol was approved by Institutional Review Boards at the Kenya Medical Research Institute, Duke University and the University of California. All participants gave their written informed consent to participate in the study prior to data collection. For low-literacy participants, consent was affirmed with thumbprint.

Results:

Between February and December 2016, 5898 women underwent cervical cancer screening in both CHC and health facilities and 1043 (17.4%) tested positive for HPV. Out of these women, 399 (38.3%) women presented for treatment at Migori County Hospital and 372 (35.6%) underwent cryotherapy. Three women were referred for LEEP and one for invasive cancer management. Among the 372 treated HPV-positive women, 273 women (73.4%) completed an in-depth interview after their treatment. The average age for participants was 37.3 yrs, for 216 (79.1%), primary school was the highest education completed, and 206 (75.4%) were married or had a current partner. There was no difference in the clinical or demographic characteristics in the participants from the original study arm, or between those who agreed to an interview and those who declined. Women traveled a mean of 37 kilometers to get to Migori for treatment, and almost all used a paid form of transportation (bus, taxi or motorbike).

Knowledge and perceptions of HPV positivity and treatment value

Many women expressed confidence in their level of knowledge about the relationship between HPV and cervical cancer, and the role of treatment in protecting their health. Specifically, many understood that the recommended treatment was simpler and more effective than it would be if HPV developed into cervical cancer.

> *"I learnt that, having HPV doesn't mean you have the disease, it is just a sign that it may develop in to a disease and when you have the virus and it is detected early enough it can be treated" (Age 41)*

Although many women were able to make fact-based statements about HPV, and professed confidence in their knowledge, some expressed fear, anxiety and misperceptions about their positive HPV results and the association with cancer. This was reflected in women's feelings around the time they received their results and their concern that the treatment would not "cure" their cancer.

> *"I felt pain at heart, since I do hear that those with cancer do not survive, even now I still have no assurance of good health." (Age 43)*

Though some women reported worry or anxiety about their test result, many felt relief that they were now aware of their HPV status and could get treatment.

> *"What came into my mind after I was confirmed HPV positive was just on how I can access treatment my focus now is how I can be on treatment and that is my key challenge as at now." (Age 47)*

Treatment Experience

Women were almost uniformly positive about provider respect, privacy, adequate explanation of the procedure and recovery, and ability to ask and have their questions answered. Most women also reported minimal pain or cramping, with no reported complications with the procedure. Overall, women expressed relief that the procedure was not as difficult as they had feared, with responses similar to the comment below.

> *"When I came from home, people were saying that this treatment is painful but I have not felt any pain. I have found it to be good and the pain that people are talking about is not there." (Age 36)*

When asked how to improve the treatment experience, women had limited suggestions, or focused on access issues. This may not reflect satisfaction with the treatment model as much as a feeling that it was the role of "health care providers or "doctors" to "improve the experience". *"It is you as healthcare providers to find on ways of making it more comfortable." (Age 33)*

Unanswered Questions

Despite reporting adequate explanation and overall treatment satisfaction, a number of unanswered questions or misperceptions regarding cervical cancer or follow-up arose throughout the interviews. When asked whether women had unanswered questions at the end of the screening/notification and treatment process, they revealed underlying fears about extent of disease/outcomes of treatment (future fertility, death from cancer, etc). Many women were under the impression that they would be given drugs to treat HPV, like treatment for malaria or HIV management. *"I have learnt that in case I will be given drugs then I will have to take them to help prevent the virus from advancing into cervical cancer" (Age 38).* Women who mentioned drugs recounted that they were *told* they would be given drugs, although this was not an intended part of the health messaging during screening or treatment.

Some women believed that if they were infected with HPV, they would not be able to give birth, or they should not get pregnant because the fetus would be infected with HPV. Related to the fear of infertility, women reported believing that family planning methods caused their positive

HPV result or would cause cervical cancer.*"I thought that I had cervical cancer because since I went for family planning [IUCD]. I have not been feeling okay in the uterus." (Age 42)*

Identifying Specific Barriers and Facilitators to Treatment Access

When women were asked whether they encountered any barriers or difficulty accessing treatment, and most answered no. However, when prompted, many confirmed that they had to miss work, struggled to find childcare or transportation funds, or traveled a long distance. Some women expressed the belief that if a woman is sick or valued her health, there were no barriers that could stop her from accessing treatment in statements like the following: *"It can only be far for someone who is not sick but if you are sick, you cannot say that it is far. I'm here to save my life" (Age 46).*

Lack of access to means of transportation and/or funds to hire transport were the main barriers that resulted in delays in treatment. Women also worried about future transport costs if the disease progressed, explicitly stating that they anticipated missing future appointments.

> *"I do not know what to tell you. If you have money you can access everywhere, but if you do not you cannot make it on foot. The poor will die of even diseases that can be treated unlike the rich." (Age 38)*

When asked about how to make treatment access easier, many women mentioned that telling their own story of treatment to women who tested positive for HPV would be helpful, suggesting that peer education and social support may play a large role in decision to get treated. Women wanted to publicize that treatment was free, easy, quick and important for women's long-term health. Examples of these sentiments include the following:

> *"When the [positive] results came I was surprised. I then took time and went to my friends who also were HPV positive and shared with them, we encouraged each other and set dates for coming for treatment." (Age 45)*

> *"I would tell her it is important for her to know her HPV status because she would be able to know if she is at a high risk of developing cervical cancer…Treatment is good. It is free and very easy. There is no pain, so it is good. That is how I would encourage her." (Age 51)*

Women suggested two changes in the treatment model that could facilitate treatment for women in the community, (1) a decentralized treatment model that provides treatment in more rural health facilities, closer to homes, or a mobile treatment unit that moves periodically through communities and (2) transportation provisions or reimbursements, echoing the main barrier to treatment access.

Finally, a substantial number of women felt that greater awareness of or access to *screening* would increase uptake of treatment. Women suggested repeating screening in the communities for those who had missed earlier campaigns and increasing involvement of lay health workers, or community health volunteers, in outreach and education around screening.

Support from Peer Networks and Community Leaders

Women wanted to share their diagnosis with others in their community, both to be able to obtain psychological and financial support for treatment and to set an example. Most reported that privacy around their HPV status was not important to them.

> *"I am comfortable with any other person knowing my status because, he or she might be able to support me if am sick or I might be able to encourage and support a person who is sick but is too scared to receive treatment."*

A small minority of women who did not want to share their diagnosis with others, apart from their spouse or co-wives, gave reasons including a general desire for privacy about their own health, without specific mention of HPV or cervical cancer related stigma.

> *"The reason why I did not want anyone else to know is because some people tend to exaggerate things, if one hears you have this disease, they may start telling you how you have a very bad disease and that you will die soon"*

Women held contradictory opinions regarding the role of community leaders in facilitating treatment. Women who were in favor stated that leaders could "*mobilize women to seek treatment"(Age 33),* while those opposed feared a loss of privacy, stating that *"community leaders would spread rumors to the community members" (Age 37)*

Male Partner Involvement

Male partner involvement was described as it related to treatment access, post-treatment care and fears of reinfection from their partners. Almost all women interviewed said the decision to seek treatment was theirs alone. However, they did feel like male support or opposition played a role in access of treatment services. Interestingly, most women stated that while men in general would likely not be supportive of their wives obtaining treatment, their own spouse had been. Reasons for other husbands' perceived lack of support were related to a lack of understanding or belief that HPV is a real threat, and low prioritization of their wives' health. Male support was generally described as financial support for transportation, with a minority naming encouragement or moral support for treatment. Women's comments indicate either a perception about lack of male support for other women in the community, while descriptions of their own experience suggest that male support was a key factor in their ability to obtain treatment (as all the women in this group had successfully obtained treatment).

> *"My husband support[ed] screening so that should I be confirmed positive, I start the treatment in time before it worsens…he provided me with fare and asked me to leave early so I can get to the hospital in time." (Age 42)*

> *"Some do not understand cervical cancer and some just care less about their wives and cervical cancer hence not becoming supportive. Other men are supportive when they*

> *value the lives of their female partners." (Age 33)*

Standard counseling after cryotherapy includes abstinence for a month, and use of a condom after resumption of sexual activity for six months to prevent spread of HPV or reinfection. A few women expressed concern about cultural and social beliefs regarding sexual activity that would prevent their husbands from supporting them through the recovery period, or use of a condom afterwards. Some women even requested that a health provider speak with their husband.

> *"I had a concern with the issue of not having sexual contact with my husband for a month. We built a new house, which we are supposed to enter into in the course of this week. As Luos, we have our customs that we must uphold, what will I do?" (Age 35)*

Concerns about the ability to be abstinent following treatment were echoed in some women's thoughts about the futility of treatment in situations where they perceived little control over possible reinfection. Concerns were raised about safe relations with their husband, inability to negotiate condoms and concerns about [re]infection among co-wives.

> *"It is said that men are the one who infects us, and us still being a young couple we are bound to have sexual relations, what can be done so to men so that they do not spread the disease?"(Age 39)*

> *"Supposing I have a co-wife, how will I know that she has also been treated so that we can all be free and not use condoms?" (Age 34)*

Treatment and Empowerment

Although this group of women who were able to overcome barriers and access treatment for their HPV likely had higher baseline levels of empowerment than women who did not get treatment, any women expressed a sense of personal empowerment from the process of either undergoing treatment or from gaining an understanding of the impact of HPV on their health. This may have played as a key factor in overcoming barriers to treatment.

> *"I have come to seek treatment for a better future; I want a future so that I can continue taking care of [my children]" (Age 35)*

Finally, almost all women said they would recommend treatment to other women who they knew tested HPV positive, stating that the treatment was easier than they thought, free, quick and almost painless. Importantly, many felt that they had an important role to play as peer educators or advocates to convince other women who tested HPV positive to get treatment. Often, women expressed that their treatment experience changed their minds about privacy and the importance of sharing their experience.

> *"I never felt like letting anyone know about my treatment, now that I have, I can easily encourage my neighbor to seek for treatment in case she's positive." (Age 36)*

> *"I would tell her my experience about the treatment. How easy and how painless it is. How the doctors are prepared and how they talk nicely to us. I would tell her she has nothing to fear and she should gather courage and come." (Age 41)*

Discussion:

Appropriate follow-up for HPV-positive women is a critical component in cervical cancer prevention and control; the success of programs in LMICs is often limited by attrition between screening and treatment. This study used the CFIR framework to explore the contextual factors surrounding women's uptake of treatment after a positive HPV test in rural Kenya. We found that women were generally satisfied and even empowered by their treatment experience. The results also showed that the belief that the treatment they were seeking would have an important and positive impact on their health enabled women to overcome the barriers of fear, lack of transportation funds and distance to the treatment center. Women's responses were surprisingly consistent throughout the interviews, with some level of disagreement emerging around the importance of male involvement in their own ability to seek treatment compared to their perception of how it impacted other women.

These findings add substantially to a body of work that has primarily focused on structural, financial, and policy-related barriers and facilitators to the implementation of cervical cancer screening and treatment programs by exploring the patient experience from receiving results to navigating treatment access.[17, 18] The participant perspectives provide important insight into ways the treatment model can be improved. To our knowledge, this is the only study to assess patient-level factors impacting cryotherapy treatment in a low-resource setting using the CFIR framework. The use of a standardized framework is important to developing a sustainable and effective enhanced linkage to treatment strategy with the potential for replication in other settings.

The fact that empowerment associated with treatment emerged so strongly was encouraging and indicated a facilitating culture. However, substantial logistical and financial barriers remain in place for women in this model, despite free screening and treatment. Women traveled an average distance of over thirty kilometers and almost all women required some form of hired transportation. While the majority of women did not recall income loss, or reported a loss of less than 1000 Kenya Shillings ($10 US), the cost of transportation represented a significant burden, even among this group of women who were not lost-to-follow-up. Partner support was significant, and most often appeared in the form of payment for transportation. While almost all women stated that the decision to seek treatment was their own, their reliance on partners for financial support was crucial and may have important implications for future cervical cancer prevention and treatment initiatives. The role of partner support needs to be explored among women who were not able to obtain treatment. The frequency at which the costs of transportation to a distant treatment site and the reliance on partners were reported indicates a need to explore the decentralization of treatment with or without a mobile treatment unit, the use of transportation vouchers, or assistance of some type that emphasized transportation.

The use of peer educators to help encourage and facilitate treatment access may also be a strategy to overcome the logistical hurdles using an empowerment framework. While other studies have not shown educational interventions to be as effective as other implementation strategies for cervical cancer prevention,[19] peer-led counseling has increased perceptions of screening benefits and engagement in screening activities.[20, 21] Peer-to-peer education has played a large role in the success of HIV programs in this region, so participants were likely to have experience and comfort with this. Importantly, women saw themselves as potential peer educators, using their positive experiences with treatment to convince other women to get treated. In this way, the self-efficacy they displayed in obtaining treatment would be transformed into a sense of personal empowerment through a reflection of their own success and influence on others.

This qualitative data clearly elucidated points of clarification for the educational counseling provided throughout the outreach, screening and treatment activities. Although the current education modules stress that HPV is not cancer, some women continued to believe that a positive HPV result was synonymous with having cancer, which then caused cancer-related fear, sometimes resulting in inaction. Educational content and the mechanisms by which women are notified of their results should be rigorously tested to ensure clarity, as fear of cancer or more invasive procedures may prevent women from seeking appropriate treatment. In addition, these data highlight a need to address the misconceptions about family planning, infertility, and the need for medication as part of treatment both during outreach and at the time of screening and treatment. The persistent expectation that treatment would involve long-term medications may reflect an interpretation of medication as synonymous with treatment, as is the case with the more common diseases in the area: HIV, TB, and malaria. Based on these findings we updated the educational material to include more precise descriptions of the cryotherapy procedure and clarify that treatment does not require medication.

While this data highlighted crucial information that allows us to further understand how and why women are able to access treatment when free treatment is offered, there are limitations inherent to the study design. The current study is missing the voices and experience of women who were unable to access treatment, who were the majority of women screened; this may contribute to the relative homogeneity of observed themes. For example, in this population of women who had successfully accessed treatment, almost all were in a relationship or married, which was possibly a key factor in their success with navigating treatment. While the qualitative data suggests partner financial support was key in reaching treatment sites, we must identify and work with women who were lost-to-follow-up to fully begin to understand and address insurmountable barriers. In addition, as these interviews were done by the study team in proximity to treatment sites, there may have been some social desirability bias in responses related to treatment experience and provider respect.

Conclusions

These data provide valuable insight on the implementation of a community-based cervical cancer screening program through the perspectives of HPV-positive women who were able to access free treatment through referral to a county government hospital. While many women reported feelings of self-efficacy and empowerment, and were pleased with their experience deciding and accessing treatment, they represent the minority of patients. Despite multiple efforts to counsel women about the importance and availability of treatment, over half of the women who tested HPV-positive in the parent study did not access treatment. We have identified specific barriers and potential facilitators to treatment access that will inform new implementation strategies and ways to intensify efforts to reach the wider population of women who were lost-to-follow-up and work with health care teams to develop a linkage to treatment strategy that ensures greater follow-up with appropriate care.

List of abbreviations:

CFIR: Consolidated Framework for Implementation Research

HIV: Human Immunodeficiency Virus

HPV: Human papillomavirus

IDI: In-depth Interview

TB: tuberculosis

WHO: World Health organization

Declarations:

Ethics approval and consent to participate:
The KEMRI Scientific and Ethics Review Unit (SERU; #2918), the Duke University Institutional Review Board (Pro0007742) and and the University of California San Francisco (UCSF) Human Research Protection Program Institutional Review Board (14-13698) reviewed and approved the study. All participants gave their written informed consent to participate in the study prior to data or specimen collection.

Consent for publication:
Not Applicable

Availability of Data and Materials:
Deidentified participant data and coding reports are available at request from Dr. Huchko (ORCID # 0000-0002-4081-4768) for up to ten years with permission of the Duke and KEMRI ethical review committees.

Competing Interests:
The authors declare that they have no competing interests

Funding:
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Authors' contributions:
MJH is the overall study PI. She conceived the study, led the study design, led the coding and analysis, and wrote the manuscript. KA, SY and SI assisted with the coding, analysis and conceptual framework. SY lead data collection activities. SI led data management. EB assisted with the manuscript preparation and acts as the site PI. All authors have read, actively edited and approved the final version of the protocol.

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Reporting checklist for qualitative study.

Based on the SRQR guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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		Reporting Item	Page Number
	#1	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	1
	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	2
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	4, 5
Purpose or research question	#4	Purpose of the study and specific objectives or questions	5
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The	6

		rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	6
Context	#7	Setting / site and salient contextual factors; rationale	5
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	5
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	7
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	6
Data collection instruments and technologies	#11	Description of instruments (e.g. interview guides, questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	6
Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	7
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	6
Data analysis	#14	Process by which inferences, themes, etc. were identified and	6

		developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	6
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	7-13
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	7-13
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	13
Limitations	#19	Trustworthiness and limitations of findings	15
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	17
Funding	#21	Sources of funding and other support; role of funders in data collection, interpretation and reporting	17

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