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Video Colposcopy for Decreasing Anxiety in a Low-Income Setting

Jessica Zheng
Yale Physician Associate Program, jessica.zheng@yale.edu

VIDEO COLPOSCOPY FOR DECREASING ANXIETY IN A LOW-INCOME SETTING

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Jessica Zheng PA-SII
Class of 2020
Yale Physician Associate Program

Sangini Sheth, MD, MPH
Assistant Professor of Obstetrics,
Gynecology and Reproductive Sciences
Yale School of Medicine

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Abstract

Cervical cancer is the fourth most common cancer and fourth most common cause of cancer-related death in women in the world. Current guidelines for cervical cancer screening recommend a Pap and/or human papillomavirus test and a follow-up colposcopy if particular abnormalities are discovered. In many patients, colposcopies cause significant levels of anxiety, adversely impacting patients' pain tolerance and adherence to follow-up. Previous studies have shown mixed results on whether video colposcopy decreases this anxiety. Moreover, these effects have not been assessed in low-income communities who are disproportionally affected by cervical cancer. **In this study, we will conduct a single blind randomized controlled trial to determine whether video colposcopy decreases anxiety associated with colposcopy in low-income patients.** This study may help demonstrate the effectiveness of video educational interventions in reducing anxiety, potentially establishing video colposcopy as a useful addition to standard colposcopy practice in this patient population.

Chapter 1: Introduction

1.1 BACKGROUND

Cervical cancer is a slowly developing cancer that is most commonly caused by persistent infections with the human papillomavirus (HPV) and is largely preventable with the HPV vaccine. Currently, it is both the fourth most common cancer and the fourth most common cause of cancer-related death in women across the globe with a current estimated incidence rate of 13.1 per 100,000 and a prevalence of about 1,939,000.[1-4] In 2015, this cost the United States an estimated $3.3 billion due to direct healthcare costs and lost productivity costs from missed work or early death.[5]

Since the 1950's, the incidence of cervical cancer and its associated mortality has significantly decreased in the United States. For 2020, the American Cancer Society estimates that there will be 13, 800 new cases and an estimated 4,290 deaths due to cervical cancer.[6] This decrease in disease burden is largely due to the success of early detection and screening programs with HPV testing and the Pap test which can identify precancerous lesions called cervical intra-epithelial neoplasia (CIN) before it progresses to invasive cervical cancer.[7] Abnormal findings are often followed up with colposcopy where the cervix is visualized. During the procedure, cervical biopsies, endocervical curettage, or treatment may also occur if warranted. In the last few decades, this downward trend has stagnated indicating the need for improvements in rates of screening, in the screening test itself, and in subsequent evaluation and management of abnormal screening results.[6] One aspect requiring improvement is the significant level of anxiety women experience during all stages of the cervical cancer screening process, and especially during colposcopy. [8-11] As this anxiety often leads to several adverse consequences including decreased pain tolerance and subsequently

suboptimal adherence to critical follow-up care, further research and development into effective interventions to decrease anxiety is warranted to improve these health outcomes.[12-15]

In previous studies, it has been shown that the anxiety associated with colposcopy is due to several factors. Some of the factors include inadequate understanding of cervical cancer screening, fear of pain or discomfort during the procedure, worries about sexual dysfunction, and fear of potentially having cancer.[9-11,13,16] One study found that some women thought that coming in for a Pap smear meant that their medical provider thought they had cancer.[17] Other studies have found that women thought that cervical cancer was either incurable or unpreventable.[17,18] With these beliefs about cervical cancer screening in mind, it is not surprising that in 2003 the National Assessment of Adult Literacy found that only an estimated 12% of Americans had proficient health literacy with the majority of Americans having intermediate health literacy with basic health information and services.[19] This is especially concerning as past research has demonstrated that patients with poor health literacy experience higher anxiety and distress levels.[20,21] Thus, the data strongly suggests that providing more information about colposcopy and the cervical cancer screening process, and using tools that increase patient engagement could potentially reduce anxiety levels in these patients.

As such, several studies in the past have attempted to decrease this anxiety using educational and information sharing interventions. These interventions include information leaflets, informational videos, pre-colposcopy counselling, and individually targeted information.[8,22-28] Of the studies that looked at the utility of providing informational leaflets before colposcopy, one smaller study found that providing women with a simple booklet of

information reduced anxiety while other larger studies found that their informational leaflet did not provide any anxiety relief.[24,25,28] Inconsistent results have been similarly reported in studies looking at informational videos prior to colposcopy: one study showed a significant decrease in patient anxiety while two others showed no significant decrease in patient anxiety levels.[8,22,29] Providing pre-colposcopy counselling or individually targeted information over the phone and in the mail found negligible effects on reducing anxiety levels as well.[23,26,27,30] Ultimately, a 2011 Cochrane review of six randomized controlled trials conducted by Galaal et al., concluded that of these interventions, only watching an informational video in addition to an information leaflet showed any significant effect on decreasing anxiety levels in women undergoing colposcopies.[31]

Alternative strategies for decreasing patient anxiety include the use of music and mind-body interventions. It is hypothesized that these tools may be effective not as a way to provide additional knowledge, but either as a means to distract or calm those undergoing colposcopy. One study conducted in Chinese patients found that the use of slow rhythm music significantly decreased patients' anxiety levels as measured through the Spielberger State Trait Anxiety Inventory (STAI).[32] Similar results are reported in another study conducted among adolescents that found that music videos decreased patient's body movements indicative of pain or distress during the colposcopic examination.[33] However, recently there have been several studies reporting the opposite result.[34-37] A systematic review and meta-analysis of five randomized controlled trials on the effect of music therapy by Abdelhakim et al. concluded that music had no significant effect on decreasing anxiety levels in patients presenting for colposcopy.[38] However, it should be noted that none of these studies utilized the same types of music during the colposcopic exam, possibly explaining the

heterogeneity of results.[32,34-37] Mind body interventions like guided imagery have also found no effect on reducing patient's anxiety levels.[34] Thus, current available evidence for the use of distraction or calming tools during colposcopy indicates that they are at best, minimally effective in reducing patient anxiety levels.

The use of video colposcopy as a tool to decrease patient anxiety shows some potential. Thus far, only a few experimental studies have investigated its effectiveness with variable results. One study conducted by Walsh et al. found that the use of video colposcopy in consecutive colposcopies significantly decreased self-reported anxiety levels during the colposcopic examination in a group of patients in Ireland.[14] Another study found the same result but only in a subset of patients who scan for threats and seek out information in response to psychological stress.[39] Two other studies have found results inconsistent with these findings. The study conducted by Rickert et al., who studied adolescents, found that video colposcopy did not result in significant STAI score differences between the video colposcopy group and the control group.[33] Similarly and more recently, in a large randomized controlled trial, Hilal et al. found that video colposcopy had no significant effect on reducing anxiety levels in German women presenting for first time colposcopy measured using the STAI before and after the colposcopic exam.[40] This heterogeneity of results might be explained by the different patient populations studied in these trials as well as methodological differences in the study designs. Demographic characteristics in several of these studies did not include race, ethnicity, or socioeconomic status and so comprehensive comparisons between the studies are unable to be reliably drawn and extrapolated into other patient populations. In light of these variable results, incomplete demographic data, and

protocol differences, further investigation is needed to determine if similar effects will be seen with the use of video colposcopy across different patient populations.

As the majority of these studies were conducted in Europe, whose patient populations are considerably different from the U.S., the utility of video colposcopy as a strategy to decrease anxiety in low-income patients is still unknown. Evidence in the literature suggests that culture has significant influences on how individuals experience anxiety, suggesting that patient populations from different cultures may react to video colposcopy differently as an intervention to reduce anxiety.[41,42] Moreover, none of these studies have looked at low-income populations in the U.S. who are predominantly racial and ethnic minorities who have the highest burden of cervical precancer and cancer in America.[43-45] This highlights the need for more research into these vulnerable groups. According to the article by Singh et al, from 2009-2013, women in the lowest socioeconomic status (SES) bracket had a 76% higher cervical cancer mortality rate than women from the highest SES bracket.[43] Health disparities by race and ethnicity also continue to persist in cervical cancer statistics in the U.S. As of 2016, incidence rates and mortality rates from cervical cancer have been found to be higher in black women and Hispanic women compared to white women at 8.7 and 9.8 versus 7.5 per 100,000 and 3.1 and 2.7 versus 2.1 per 100,000, respectively.[45,46] Poor health literacy also afflict these low-income and minority populations illustrating the urgent need to identify interventions to target their lack of knowledge and in doing so, decrease their anxiety upon presentation for colposcopy.[47-49] Fortunately, previous research has demonstrated that the use of culturally sensitive and targeted video technology can help increase patient knowledge and overcome barriers posed by limited education .[8,50-54] Based on this data, further investigation

into video colposcopy is warranted to evaluate whether it is a useful intervention to decrease anxiety in these low-income patients undergoing first time colposcopy.

1.2 STATEMENT OF THE PROBLEM

A few randomized controlled trials to date have examined video colposcopy as a potential tool to decrease anxiety in patients presenting for first-time colposcopy. Previous studies have produced mixed results on its efficacy with some studies demonstrating a benefit with video colposcopy and others demonstrating none. However, these current studies are limited in the interpretation of their results as several of them feature design elements that introduce sources of bias and are limited in generalizability. These design elements range from using a poor method to randomize patients to failing to account for certain confounders. Moreover, each of the four published randomized controlled trials studied a different population of interest and failed to report important sociodemographic information on their sample populations.[14,33,39,40] Given the limited external validity of these studies, the utility of video colposcopy to decrease anxiety remains unknown in low-income and minority patients who are disproportionately affected by cervical cancer in the United States. The proposed study will be a randomized controlled trial to determine the efficacy of video colposcopy in reducing anxiety in a population who is grossly understudied and has the potential to benefit greatly from the results.

1.3 GOAL AND OBJECTIVES

The goal of this proposal is to determine whether video colposcopy is a useful tool to effectively decrease anxiety levels in low-income women undergoing colposcopy for the first time. The proposed study will evaluate whether the use of video colposcopy as an interactive information sharing tool during the colposcopic exam will lead to a significant reduction in

anxiety levels compared to standard non-video colposcopy and improve adherence to follow-up in these patients. The primary outcome will be the mean reduction in anxiety. Patient adherence to follow-up, patient satisfaction, patient knowledge of colposcopy and cervical dysplasia, and patient pain during the colposcopic exam will also be measured to determine if video colposcopy improves these secondary outcomes. This study ultimately hopes to inform colposcopy practice on a way to decrease anxiety in first time colposcopy patients.

1.4 HYPOTHESIS

We hypothesize that low-income patients presenting for first time colposcopy randomized to video colposcopy will have a different mean change from baseline in the Spielberger State Trait Anxiety Inventory (STAI) when compared to those patients undergoing traditional non-video colposcopy.

1.5 DEFINITIONS

Video Colposcopy: Video colposcopy utilizes a video colposcope to enable both the clinician and the patient to view in real time, the cervical examination that is being performed on a television monitor.

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Chapter 2: Review of Literature

2.1 INTRODUCTION

We conducted a comprehensive search from the following databases between June 2019 and May 2020: PubMed, Ovid MEDLINE, EMBASE, and PsycINFO, Cochrane Library, Scopus, and Sociological Abstracts. The following terms or a combination of these terms were used to search for relevant literature: *colposcopy, video colposcopy, colposcope, anxiety, State Trait Anxiety Inventory, fear, pain, cervical cancer, cervical cancer guidelines, anxiety across cultures, adherence, patient satisfaction, patient knowledge* and *health literacy.* Key terms used to search for protocol and methodology specific determinations included: *confounders, side effects, and safety*. Articles in the English language or English translations were evaluated for theoretical soundness, strength of design, and significance of data. Pertinent articles were included and further analyzed in this review.

2.2 CERVICAL CANCER, SCREENING, AND ANXIETY

Cervical cancer occurs when cells in the cervix undergo abnormal changes most commonly caused by oncogenic strains of the human papillomavirus (HPV). This process usually occurs over several years and therefore most women who are diagnosed with cervical cancer are usually between the ages of 44 and 68.[1] Because this cancer develops over a relatively long period of time, it is one of the very few cancers that is largely preventable with the HPV vaccine and cervical cancer screening programs.

The cervical cancer screening process begins at age 21 for women in the U.S. The U.S. Preventative Task Force currently recommends that women aged 21-29 receive a Pap test every 3 years and women aged 30-65 screen with a Pap test alone every 3 years, high-risk HPV testing alone every 5 years, or cotesting every 5 years.[2] Following a Pap test, if

certain abnormalities are found, women are subsequently referred for a colposcopy, a standard diagnostic procedure that uses a stereoscopic binocular microscope to visualize the cervix and obtain biopsies of any areas suspicious for neoplasia. In the literature, it has been well documented that women experience significant levels of anxiety both before and during this procedure.[3-7] As this anxiety with colposcopy has been associated with decreased pain tolerance, psychosocial and psychosexual dysfunction, and decreased adherence to follow up, various interventions have been developed to help provide anxiety relief in these patients.[7-12]

2.3 REVIEW OF PREVIOUS INTERVENTIONS TO REDUCE ANXIETY

Several strategies have been investigated to help decrease anxiety in women attending their first colposcopy with educational and distraction or calming interventions being the most studied. The following detailed review consists of several trials that have tested the utility and efficacy of these interventions.

Informational Leaflets and Booklets

One strategy used to decrease anxiety has been to provide informational leaflets or booklets to patients prior to colposcopy. Three studies to date have investigated their use with varied results. One small study (n=64) conducted by Marteau et al., showed that sending a simple informational booklet in the mail prior to colposcopy that contained procedural information, behavioral instructions, and outcome information significantly decreased patients' anxiety.[13] In the study, there were 4 different groups. Group 1 underwent routine care, Group 2 was sent a simple informational booklet, Group 3 was sent a complex informational booklet, and Group 4 was sent both booklets. Anxiety was measured using the state scale of the Spielberger State Trait Anxiety Inventory (STAI), a validated scale of anxiety that utilizes a 20-item questionnaire and a 4-point Likert scale. [14] Scores range from

20-80 with higher scores indicating higher anxiety. Scores were compared at two time points: upon receipt of the colposcopy appointment and right before colposcopy. The first STAI scores were taken after receipt of any booklets in the mail.

The STAI scores of the groups were as follows upon receipt of appointment: Group 1=46.2, Group 2= 43.9, Group 3= 46.8, and Group 4=38.3, $p < .05$. The following STAI scores were those obtained at the appointment: Group 1= 50.7, Group 2= 44.8, Group 3=49.1, and Group 4=42.1, $p < .025$. At both time points, Group 2 and Group 4 had significantly different mean STAI scores compared to Groups 1 and 3. The authors thus concluded that those groups that received the simple informational booklet were less anxious after receipt of the simple booklet compared to those groups who did not receive it.

However, while this study demonstrates some significant anxiety reduction with an informational booklet, there are some limitations to this study. One limitation is the absence of confirmation that the women who were sent the informational booklets in the mail actually read them. Thus, caution must be taken to attribute the differences in anxiety to the simple informational booklet alone as it is possible the women also relied on other sources of information. Another limitation is the small number of participants in each group (Group 1: n=13, Group 2: n=21, Group 3: n=15, and Group 4: n=15) as well as the absence of sample size calculations. These aspects of the study call into question whether this study was powered correctly to detect a clinically significant effect size.

Two larger randomized controlled trials evaluated the provision of informational leaflets or handouts prior to colposcopy and found results contrary to those found by Marteau et al.[15,16] Tomaino-Brunner et al. (n=113) conducted a quasi- randomized controlled trial assessing the effect of an educational intervention on knowledge and anxiety in patients

scheduled for a colposcopy. This study found no significant difference in STAI scores between those who received an educational handout in the mail one week prior to the colposcopy and those who did not.[15] STAI scores prior to the colposcopy in the intervention group and the control group were 47.9 ±12.8 and 50.8±13.3, respectively. The difference in STAI scores was not found to be significant (p-values were reported as nonsignificant but no specific values were reported). However, it should be noted that the authors powered their study based only on knowledge of colposcopy and not on STAI scores. Based on a previous study the investigators had conducted, they found that only 30% of women knew what a colposcopy was and used this percentage as their estimated effect size in their sample size calculations.[15] One methodological weakness of this study includes the method of allocation which used a randomization scheme based on the week of scheduled appointment rather than a truly random allocation, increasing the risk of selection bias. The lack of a pre- and post-test design also makes it hard to determine if the handout was truly the variable that produced the end results. The results of Howells et al. support those found by Tomaino-Brunner et al. In a prospective randomized controlled trial (n=200), they found that the provision of informational leaflets prior to colposcopy did not produce a statistically significant difference in STAI scores between the intervention and control groups, either before colposcopy or at the 6-month follow-up visit.[16]

It should also be noted that the studies conducted by Marteau et al. and Howells et al. are limited in terms of their external validity as neither study listed demographic information concerning race and ethnicity or SES. Thus, the generalizability of their results to other patient populations is unknown at this time. Overall, the results of these studies are

inconsistent and inconclusive regarding the efficacy of these interventions in reducing anxiety.

Pre-colposcopy Informational or Counseling Sessions

Pre-colposcopy information sessions with counselling have been evaluated in three randomized controlled trials but have shown negative results. In a quasi- randomized controlled trial conducted by Sarkar et al. (n=59), women who received an even hospital number received counseling by the clinic nurses before filling out a questionnaire about anxiety and depression.[17] Women who received an odd number filled out the questionnaire before they received counselling. Anxiety was measured using the STAI and no significant differences between the mean STAI scores were seen between groups. In two other studies (n= 147-220), informational leaflets and video information were provided to both the intervention group and the control group prior to colposcopy. [18,19] In addition to these resources, an additional discussion with an experienced colposcopy nurse was provided in the study by Chan et al. and pre-colposcopy group sessions with a colposcopy nurse was provided in the study by Byrom et al. to the intervention group. No significant differences in mean STAI scores between groups were detected in either of the studies.[18,19] The mean STAI score in the study by Chan et al. prior to the colposcopic examination was 45.21±11.88 in the intervention group and 45.81±9.89 in the control group.[18] In the Byrom et al. study, the mean pre-colposcopy STAI score was 46.36± 11.98 in the intervention group and 45.94 ± 13.99 in the control group. However, the study conducted by Byrom et al. did not recruit enough participants to achieve their sample size to power the study. Thus, the study may not have been large enough to detect the effect size. Similar to previously mentioned studies, all three studies are limited in generalizability of their results as the study conducted by Chan et al.

only recruited Chinese patients and the studies conducted by Sarkar and Byrom et al. did not report race and ethnicity or SES data.

Targeted Information

As anxiety can be quite individualized, one randomized controlled trial published in 2011 by De Bie et al., looked at whether targeted information through the mail or telephone would provide any anxiety relief to these women. [20] Women who were randomized to the intervention group received a phone call that included topics about the Pap result, precancer versus cancer, the colposcopic procedure, treatment, HPV, HPV vaccination, and fertility. They also received a document that included information about the screening program, abnormal smear results, and steps after an abnormal smear result. The control group received a 2-page informational leaflet that included information about colposcopy and treatment. Anxiety was measure using the STAI on arrival to the colposcopy clinic. The median STAI score for the intervention group was 48.0 (42.0-56.0) and the median STAI score for the control group was 50.0 (40.0-59.0), p=0.92. Thus, no significant difference was found between the median scores between the intervention group and the control group with targeted information over the phone and in the mail.

Informational Video

Studies conducted by Freeman et al., Ketalaars et al., and Wouters et al., have assessed the utility of an informational video as a medium to decrease anxiety. The earliest of these studies (n=93) by Freeman et al. in 2001, utilized a 7-minute clinic-specific video that included information about abnormal Pap smears, the consultation, and possible treatments.[4] This videotape and a standard explanatory leaflet were sent to women in the intervention group prior to their see and treat colposcopy appointment and only the explanatory leaflet

was sent to the women in the control group. Anxiety was measured using the STAI at the woman's first attendance to the clinic. The mean STAI score of those who received the video and the leaflet was 43.2 ±12.09 while the mean STAI score of those who only received the leaflet was 54.7 ± 12.58, P=.00004. The authors therefore concluded that the video significantly reduced their patients' anxiety. The videotape cost £1.50 for each woman in the video group making it more likely that these women did indeed watch the video compared to if the videotape was free. This is because there is a monetary loss if the women choose not to watch the video. However, there was no formal verification that the women who received the videotape actually watched the video. Thus, these results must be interpreted in the context of this limitation.

Two recent larger randomized controlled trials provide contradictory results to those found by this study. In 2017, Ketalaars et al. (n=136) examined the efficacy of an 11-minute video prior to colposcopy in decreasing anxiety. The content of the video was very similar to the one used by Freeman et al., and included hospital and clinic specific images as well as explanations of abnormal smears, the consultation, and possible treatments.[21] Women randomized to the intervention group received a link and password through the internet for the online video and the standard informational brochure through the mail and women randomized to the control group only received the standard informational brochure. The primary outcome was difference in anxiety between the groups as measured by the STAI and the Hospital Anxiety and Depression Scale (HADS). The mean STAI score after the invention in the video group was 44.3± 10.7 while the mean STAI score in the control group was 44.9± 11.0, p= .752. The mean HADS anxiety score after the intervention in the video group was 6.2±4.4 while the mean HADS score in the control group was 6.7±4.6, p=.491.

Neither of these measures was found to be statistically different between the two groups and the authors concluded that video information did not reduce anxiety levels in women referred for their first-time colposcopy.

The results of the previous study are supported by Wouters et al. In 2019, Wouters et al. (n=122) studied the effect of a hospital-independent animation video on consultation time, anxiety and satisfaction.[22] The methods of this study were similar to the prior studies. The animation video included information on different cytology results, the colposcopy procedure, possible treatments, possible side effects, and follow-up procedures. Women in the intervention group received this video and standard written and oral information on colposcopy and the control group just received the written and oral information prior to colposcopy. Anxiety was measured via the STAI and the HADS. The pre-colposcopy mean STAI score in the animation video group was 46.8± 10.4 and was 44.2±10.6 in the control group, p=0.16. The pre-colposcopy mean HADS anxiety score in the animation video group was 4.0 (2.5-6.0) and 4.0 (2.8-5.3) in the control group, p=0.58. Thus, no significant difference in mean STAI or HADS was observed between the two groups.

In reviewing these three studies, it should be noted that all three studies are either limited or uncertain in terms of their external validity. Freeman et al. conducted their study in London, England, and only state that there are no differences between the two groups but failed to display any demographic information. Thus, it is unknown whether the results they see in their study can be applied to other populations of women. The same problem limits the generalizability of the studies done in the Netherlands by Ketalaars et al. and Wouters et al. as they both fail to report the race and ethnicity or SES of their participants. It could be argued then that the difference in results is due to different patient populations. Thus, with

the information that is currently available, no definitive conclusions on video interventions can be made on reducing anxiety in the population of women we will be studying, as the populations studied thus far are not representative of those in the U.S.

Music

In addition to educational interventions, a few other distraction or calming tools have been evaluated to provide anxiety relief. Several studies have looked at music.

One of the first studies looking at music was conducted in 1994 by Rickert et al. who conducted two consecutively occurring studies that examined the effect of music videos and video colposcopy on decreasing anxiety in adolescents presenting for colposcopy.[23] The results of the video colposcopy study will be discussed later in the section titled "Overview of Video Colposcopy." In the study assessing music videos, 30 patients aged 13-20 were randomized to either the music video group or to the control group. The music video was selected prior to the exam and each participant watched the same music video. Several measures were used to assess anxiety including behaviors indicative of distress, the STAI, and heart rate. Some of the behaviors indicative of distress included the clinician giving reassuring comments to the patient or the patient commenting on pain. These behaviors were then coded into a list and an observer recorded the frequencies of these behaviors throughout the exam. They found that those participants in the music video group demonstrated significantly fewer behaviors and body movements indicative of pain and discomfort ($P<.003$), less reassurance from the provider ($P<.05$) and required fewer explanations from the clinician ($P<0.007$). Other behaviors, STAI and heart rate were found to be non-significant. Thus, the authors concluded that the music video had a positive effect on anxiety and distress. It should be noted that as this study was performed in adolescents who are no

longer recommended for routine cervical cancer screening, the generalizability of these results is fairly limited. Additionally, the measure that was found to be significant in this study (coded behaviors indicative of distress) is not well-validated, making the results less reliable.

A study conducted by Chan et al. in 2003 examined the effects of instrumental music to decrease anxiety in a group of 220 Chinese women and provide further support for the results found by Rickert et al.[24] Patients filled out the STAI questionnaire (translated into Chinese) prior to colposcopy and again after the procedure. Slow rhythm instrumental music was played on speakers to those women randomized to the music group. The colposcopic exam was performed by a gynecological oncologist or a gynecologist with an interest in colposcopy, but no standard format of counseling was used among these clinicians. Using mean STAI score as one of their primary outcomes, music was found to significantly reduce anxiety in women presenting for first time colposcopy. Women in the music group had a mean post-colposcopy STAI of 39.36 (95% CI 37.33-41.39) compared to women in the control group whose mean post-colposcopy STAI was 44.16 (95% CI 41.82-46.49).[24] A Cochrane review by Galaal et al. examining six studies on interventions for reducing anxiety in women undergoing colposcopy found that this reasonable large study had a low risk of bias based on its random sequence generation and concealment of allocation.[25] It should be noted however that this study was only conducted among Chinese women, utilized multiple clinicians to perform the colposcopy, and did not examine whether the music affected physician behavior and performance, in effect limiting the generalizability of the study and introducing unadjusted confounders to this study.

In contrast to the results of those found by Rickert et al. and Chan et al., many studies have found that music does not significantly decrease anxiety in women presenting for colposcopy. One study conducted by Danhauer et al. in 2007 examined the effect of music and guided imagery on decreasing anxiety in a reduced-fee colposcopy clinic.[26] The aim of their study was to determine if mind-body interventions could decrease anxiety and perceived pain. 170 women were randomized to three groups: a music group, a guided imagery group, or a usual care group. The women that were randomized to the music intervention were provided several different music options on a compact disc (CD) including classical, harp, general instrumental, or nature sounds through headphones. Women in the guided imagery intervention were provided a CD with an audio recording titled *A Meditation to Help you Be Relaxed and Awake During Medical Procedures* by Naparstek. Using mean STAI as their primary outcome, they found no significant difference in either the music intervention group or the guided imagery group compared to the usual care group.[26] Interpretation of these results should take note that 31.9% of the women recruited reported that they have had a prior colposcopy before, possibly confounding the results. Like the study conducted by Chan et al., this study also had multiple clinicians performing the colposcopy which again may bias the results.

A single-blind prospective randomized controlled superiority trial by Mak et al. in 2017 also examined the effect of music in gynecological procedures on pain, anxiety, and patient satisfaction. Patients were stratified by hysteroscopy and colposcopy. Those in the music intervention group were provided several different music options including pop, classical, and spa music which was played on an iPod with speakers during the procedure.[27] Their primary outcome was pain during the procedure measured using the Visual Analog

Scale (VAS) from 0-100 mm and one of their secondary outcomes was anxiety measured using the STAI before and after the procedure. They found that there was no significant difference in pain or anxiety between the music group and the control group. [27] One particular and unique strength of this study was that it was single blinded. Participants in the study were only told that they would be participating in a study about pain relief and not the role of music, reducing response bias. However, while this study showed no significant difference with music in lowering anxiety, a number of limitations must be highlighted. This includes the various options of music provided to the patients, the various providers who performed the colposcopy, and the lack of documentation of waiting time and duration of the procedure which all may act as confounders in this study, limiting the interpretations of these results.

Two other additional studies mirror the results found by Danhauer et al. and Mak et al. These studies conducted by Chantawong et al. in 2017 and Hilal et al. in 2018 used only one type of music to assess whether music could decrease anxiety.[28,29] Chantawong et al. played relaxing modern western style instrumental music in a stereo headset during loop electrosurgical excision procedures in 150 patients while Hilal et al. played Mozart's symphony No. 40 during colposcopy in 205 patients. The primary outcome examined in the study by Chantawong et al. was procedural pain and baseline pain scores with anxiety as a secondary outcome measured through the VAS. The primary outcome of the study conducted by Hilal et al. was reduction in mean STAI. Like previous studies, both studies did not find significant differences between the music and control groups.[28,29]

Additionally, a recent systematic review and meta-analysis by Abdelhakim et al. of these five randomized controlled trials ultimately determined that no effect was ultimately

seen with music therapy in reducing anxiety levels compared with the control group.[30] When analyzing the data, they found that there was a high heterogeneity of results. However, once the study conducted by Chan et al., was removed, this completely resolved. Thus, it seems that the results from the Chan et al. study, as mentioned previously, may be limited to the primarily Chinese population that was studied.

2.4 OVERVIEW OF VIDEO COLPOSCOPY

Previous Studies Assessing Video Colposcopy to Decrease Anxiety

To date, the specific use of video colposcopy as a tool to decrease anxiety has been studied in a few populations of interest. The first reported study in the literature assessing video colposcopy to decrease anxiety was in adolescents in 1994 in the same article mentioned previously assessing the use of music videos to decrease anxiety in adolescents.[23] This small study (n=27) recruited female adolescents aged 13-20 years and randomized them to either the video colposcopy group or the control group.[23] Multiple measures of anxiety were measured including a list of behaviors indicative of distress, STAI, and heart rate. The list of behaviors indicative of distress included items like reassurance from the clinician or comments about pain. [23] These behaviors were coded and the frequency of these behaviors was then documented during the procedure. Study participants randomized to the video colposcopy group were told they could watch the procedure on the television monitor but were not forced to do so. The only significant difference demonstrated amongst participants randomized to video colposcopy versus traditional colposcopy was that subjects in the control group provided more responses to the provider inquiring about their pain or discomfort.[23] All other measures were nonsignificant. However, several elements of the study limit the interpretation of the results. First, the authors fail to elaborate on the details of how

each patient was randomized to each group. As the study only reported that patients were randomized but not how, it is unclear if selection bias was actually eliminated. Similarly, there is no mention of whether there was any concealment of allocation, introducing another source of potential bias. The sample size of the study is also small (n=27), reducing the statistical power of the study. Furthermore, there is no mention of sample size calculations making it difficult to assess whether the study recruited enough participants to detect a difference in effect between the two groups. In terms of measured outcomes, the use of the list of coded behaviors is unvalidated, making these results somewhat unreliable. Finally, while the study reports that there were no significant baseline differences in their patients or in the other measures of anxiety like STAI and heart rate, they failed to display this data in their paper and did not speak about possible confounders and whether they were adjusted for in their analysis. Thus, while this study produced a negative result, the reported results must be interpreted in the context of these various limitations.

In 2004, one relatively small quasi-randomized controlled study (n=81), conducted in Ireland demonstrated that the use of video colposcopy in consecutive colposcopies significantly reduced anxiety in patients compared to traditional colposcopy.[10] Patients presenting for first time colposcopy were randomly assigned to the video colposcopy or control group in strict alternating rotation and the same clinician and nurse were present at each procedure. Patients were then divided into two groups based on their diagnosis on the first visit to determine the effectiveness of the video colposcopy intervention in patients with two different diagnostic conditions. One group included participants who had cervical intraepithelial neoplasia (CIN) I, CIN II, or CIN III and needed laser treatment. The other group included patients who had no abnormalities detected. Those in the former group (the

laser group) required two more visits- one for the laser treatment and another four months after receiving the laser treatment. Those who had no abnormalities detected on the first visit followed up in one year. The primary outcome was reduction in anxiety as measured by the difference in first and final STAI. In the laser group, STAI was found to be significantly reduced from the first to the final visit compared to those in the control group. Those in the laser video colposcopy group had an initial STAI of 51.82 (SD 14.22) and a final STAI of 31.86 (SD 5.56), compared to those in the laser control group who had an initial STAI of 51.62 (SD 12.56) and a final STAI of 40.29 (SD 7.06). The results of those who had no abnormalities detected on the first visit also reflect this result with those in the video colposcopy group having a first visit STAI of 49.05 (SD 11.03) and a final STAI of 34.70 (SD 6.23) compared to those in the control group who had an initial STAI of 52.33 (SD 13.46) and a final STAI of 44.78 (SD 9.89). While this study shows potential for the efficacy of video colposcopy to reduce anxiety, the study fails to provide certain details about the patients' demographic information like race/ethnicity, socioeconomic status, or pre-existing comorbidities or mental health issues. These missing patient characteristics limit the interpretation of the results as it is unsure whether any of these patient characteristics may operate as confounders. The poor method of randomization and concealment also increases the risk of selection bias as their randomization technique is not truly random and it is based on an order that can be predicted. Nevertheless, despite these methodological weaknesses this early study demonstrated that video colposcopy may be a useful tool in decreasing anxiety in patients presenting for colposcopy.

Another study by Kola et al. conducted in 2012 provides support for these results in a specific subset of patients who were identified as "high monitors", meaning those who prefer

to have more information in stressful situations.[31] In this study, the investigators assessed whether tailoring information to an individual's coping style would decrease distress in patients presenting for first time colposcopy. 117 patients were recruited for the study and divided into low or high monitors. This classification was based on their scores from the Miller Behavioral Style scale which asks patients what they would do in hypothetical threatening situations. They were then randomized to three different groups: high information, low information, and control. Those randomized to the high information group watched their examination on a monitor with a video colposcope. Those randomized to the low information group watched and listened to a DVD with nature scenes and soothing instrumental music using a head-mounted display with headphones. Those in the control group had usual care. Both physiological measures (systolic blood pressure, diastolic blood pressure, and heart rate) and self-reported measures of anxiety using the STAI were recorded before and after the colposcopic procedure. Observational measures of distress including moaning and groaning were also recorded approximately five minutes after the exam had begun. All colposcopies were done by one nurse colposcopist. They found that those patients who were high monitors experienced a reduction in systolic blood pressure from pre-colposcopy levels in both the high and low information groups. Low monitors showed an increase in systolic blood pressure during the exam compared to pre-colposcopy levels when in the high information group and a decrease in systolic blood pressure in the low information and control groups. Self-reported measures of anxiety failed to show any group differences while both high and low monitors exhibited fewer overt signs of distress in the low-information group. One strength of this study compared to the others is the use of objective measures to measure anxiety. However, they did not exclude patients who used

medications that affect blood pressure and heart rate. Thus, the interpretations of the results may be biased. Future studies will need to incorporate this exclusion criteria to provide more compelling data.

Recently, a larger prospective randomized multicenter controlled trial (n=225) conducted by Hilal et al. in Germany, demonstrated no significant reduction of anxiety with the use of video colposcopy.[32] Their primary outcome was the mean reduction in anxiety scores and was not found to be significantly different between those who had a video colposcopy and those who had a traditional non-video colposcopy (-10.3 ±11.3 SD in 111 women in the video colposcopy group and -10.3 ± 11.0 SD in 105 women in the traditional colposcopy). This study demonstrated many aspects of a well-designed RCT. The study was a multicenter study conducted in both a doctor's office setting and hospital setting expanding the generalizability of the study. Participants were given an informational leaflet to standardize medical knowledge about cervical cancer, HPV, and colposcopy; and the colposcopic exam was standardized decreasing possible sources of confounding. The method of concealment of allocation was also appropriate as they used a staff member not involved in the study to place the allocation slips into consecutively numbered opaque envelopes. They also calculated their sample size appropriately based on data from the study conducted by Chan et al. and recruited enough patients to achieve this calculated sample size.[24]

However, there are certain elements of their protocol that may help explain the negative result of their study. First, while they did use a computerized randomization tool to randomize patients, they utilized block randomization with block size four making it possible for the staff member who performed this random allocation to predict the allocation of some participants, introducing a possible source of bias. The baseline characteristics of the

participants also showed some differences that may explain why video colposcopy did not reduce anxiety in these patients. In the video colposcopy group, there were more women who had concomitant disease (48 (43.2%) vs 38 (36.5%)) and more colposcopic findings suspicious for invasion (5 (4.5%) vs 0). Women who have concomitant diseases may already have a high burden of anxiety from preoccupation with their other disease making video colposcopy less effective. Similarly, women who are told that their colposcopy found lesions suspicious for invasion may not find video colposcopy helpful in reducing anxiety due to the heightened concern for cancer. Moreover, the majority of women in the study had major changes on colposcopic exam (48.6% in the video colposcopy group and 53.8% of the control group). This may explain why video colposcopy did not decrease anxiety as the graphic nature of some of these lesions may have served to increase anxiety. Thus, this study may have benefited from a multiple linear regression analysis with concomitant disease and colposcopic findings as independent variables.

In terms of analysis, the study reports that analysis was by intention to treat but nine protocol violations occurred and these patients were not included in the final analysis; three were from the video colposcopy group and six were from the control group. Since not all randomized patients were analyzed, the data was not actually analyzed by the intention to treat principle. As this exclusion compromises the original randomization, this may be a source of bias as it may have created important prognostic differences between the groups. For example, if the six patients from the control group who were not included in the final analysis had more anxiety regarding colposcopy, this exclusion would skew the results so that the effect of video colposcopy to reduce anxiety was underestimated. The study also conducted a subgroup analysis looking at patients who were the most and least anxious. They

found that video colposcopy also did not reduce anxiety in either of these groups. However, this may be misleading as these subgroups were both small (n=55 for the most anxious patients vs n= 56 for the least anxious patients). Therefore, there may not have been enough people in each group to detect an effect size if there was one. Lastly, the generalizability of this study is limited as this study was conducted in Germany and important patient characteristics like race, ethnicity, and SES were not reported. It is therefore unclear whether these same effects would be seen in other patient populations.

Thus, so far, the existing data remains both limited and mixed on the utility of video colposcopy in reducing anxiety in patients who present for first time colposcopy.

Additional Demonstrated Benefits of Video Colposcopy

While research in evaluating the efficacy of video colposcopy in decreasing patient anxiety levels undergoing colposcopy has not produced a definitive consensus, there have been many other demonstrated benefits of video colposcopy. One significant outcome is improved adherence to follow-up care. A review of literature by Eggleston et al. identified that some of the risk factors for decreased adherence to follow-up care include race and decreased knowledge of the cervical cancer screening process.[7,33] A study looking at video colposcopy for improving adherence found significantly increased adherence rates from 50% in patients who underwent a traditional colposcopy to 80% in patients who had a video colposcopy.[34] This is a significant finding as close surveillance and follow-up after a single colposcopy is indicated even in patients in whom no or low risk abnormalities are identified. Among women with high grade cervical abnormalities found at time of colposcopy, more immediate interventions are often indicated but subsequent short interval surveillance follow up is also needed to ensure a patient has returned to a baseline population-level risk of future

cervical cancer. Other demonstrated benefits of video colposcopy include improved patient knowledge as well as improved patient satisfaction although data has been variable with the latter.[22,32,35,36]

Side Effects

The same side effects or complications from traditional colposcopy can also result from video colposcopy. These side effects or complications include: bleeding, cramping or pain, vaginal discharge, and in rare cases infection. Results from the study conducted by Hilal et al. indicate that patients experience a negligible level of discomfort and anxiety from watching the live video during video colposcopy. [32]

2.5 REVIEW OF RELEVANT METHODOLOGY

Study Design and Blinding

Currently in the literature, most of the studies assessing video colposcopy have used an unblinded randomized controlled trial design.[10,23,31,32] All of these studies assessing video colposcopy were unblinded due to the nature of the intervention. One study conducted on the efficacy of music to decrease pain during gynecological procedures used a single blind design where the participants were informed that they would be taking part in a study about pain relief but were not informed about the role of music until afterwards.[27] As our intervention is similar, a single blind study design is justified and will decrease response bias. Previous studies lack any details about the blinding of outcome assessors and data analysts, but in order to decrease any potential sources of bias, this protocol is justified and will provide the most robust evidence to assess the utility of video colposcopy in decreasing anxiety in first time colposcopy patients.

Randomization Techniques

Prior studies have used various methods to randomize their patients. One study randomized every second patient to the treatment group while another study had their patients select a random assignment slip.[10,26] An additional study randomized patients by using week of scheduled appointment.[15] These methods are not truly random as in the first 2 cases, randomization depends on an order and in the third case, is subject to seasonal or temporal variation. Consequently, these techniques may not represent the best methods to randomize patients. Another study utilized block randomization (block size 4) with a 1:1 allocation ratio. [32] While this method is more truly random, the staff member who performed the random allocation may be able to predict the allocation for later patients in the block, introducing a source of bias. Most other studies utilized a computer-generated random number series to allocate their patients to treatment or control.[16,18,19,21,24,28] As this represents a truly random method to allocation patients, this randomization technique is the most appropriate for the proposed study to reduce selection bias.

Primary Outcomes

Most studies conducted on interventions to reduce anxiety in first time colposcopy patients have utilized the Spielberger State and Trait Anxiety Inventory (STAI) to measure anxiety.[4,13,15,16,18-21,23,24,27,29,31,32] This inventory was originally developed by Spielberger et al. and is a self-reported measure of anxiety composed of 40 items- 20 items for the assessment of trait anxiety and 20 items for state anxiety.[14] Trait anxiety refers to a more constant state of anxiety that an individual exhibits whereas state anxiety refers to anxiety that is more transient and experienced in a specific time and situation. Examples of statements assessing trait anxiety include: “I am a steady person” and “I worry too much over things that don’t really matter.” Examples of statements assessing state anxiety include: “I am tense” or “I feel

calm." These 20 items on both the state and trait versions of the STAI are rated on a 4-point Likert scale. Scores range from 20 to 80 with higher scores correlating with increasing anxiety. It has been suggested that 40 be the cutoff point to detect clinically significant anxiety.[14,37] Cronbach's alpha scores have been reported to be between 0.86-0.95 for working adults, college students, high school students, and military recruits.[14] The test-retest reliability for the STAI in high school students and college students was found to be .68-.86 for trait anxiety and.16-.62 for state anxiety.[14] The low stability values for state anxiety are reasonable as it reflects a measure of anxiety in a specific time and situation. One disadvantage of this inventory is that it is a self-reported measure of anxiety. However, as various disciplines have utilized this inventory and found it to be a reliable and validated measure to detect anxiety, this inventory remains one of the gold standards to measure anxiety.[14]

Some other studies have also utilized physiological measures as a proxy to measure anxiety like heart rate, systolic blood pressure, and diastolic measure in order to supplement self-reported measures of anxiety to obtain more objective data. [23,31] However, while these measures may be more objective, heart rate and blood pressure can be affected by various factors including but not limited to medication use, disease processes, or substance use.[38] Moreover, these physiological measures are proxies of anxiety and while they show promise, they have not been well-validated to measure anxiety. Therefore, as STAI has been more widely validated as a scale to measure anxiety, we will utilize the difference in pre-colposcopy STAI and post-colposcopy STAI to measure mean reduction in anxiety as our primary outcome.

Secondary Outcomes

The secondary outcomes we will measure include adherence to follow-up, patient satisfaction, patient knowledge of colposcopy and cervical dysplasia, and pain during the colposcopic procedure.

Prior studies have measured patient adherence to follow-up in various ways. One study measured patient adherence rates and this was calculated by dividing the total follow-up visits attended by the total number of appointments made.[18] Another study measured adherence by whether or not the patient came to her follow-up or rescheduled. [34] As we are more interested into whether the patient comes to the next follow-up visit and not the overall adherence rate to follow-up appointments, we will use the latter method.

Prior studies assessing patient satisfaction using video colposcopy have used highly variable methods ranging from using ratings of satisfaction using 3-5 point scales[10,26,27] to utilizing a visual analog scale (VAS).[28,29,32] Most of these scales are not well-validated nor are they specific to colposcopy. The PEACE-q was developed by Pop et al. and is the first questionnaire developed to assess satisfaction specifically in colposcopy patients. While it has only been used in one published article and it has not been widely validated yet, it has been demonstrated to have good psychometric properties with a Cronbach's alpha of 0.76.[22,39] The questionnaire has 8 items which are rated on a 4-point Likert scale. Higher scores correspond with higher satisfaction with the colposcopy procedure. As this questionnaire demonstrates an acceptable internal consistency and is more specific to colposcopy practice, using this questionnaire is justified to assess for patient satisfaction.

In prior studies, various questionnaires and interviews were developed to assess patient knowledge of colposcopy and cervical dysplasia. One study asked "What is your understanding of an abnormal smear result"[10] while another used an interview to ask

participants open-ended questions like “Do you know why you are scheduled for this appointment?” or “What is a colposcopy?”[15] Other studies have used questionnaire formats that have ranged from true/false[31] to multiple choice.[13,18] As virtually none of these measures have been tested for their internal consistency or validity, these methods to measure patient knowledge provide insufficient evidence to determine whether they actually measure patient knowledge. One study conducted by Kola et al. utilized a 7-item questionnaire asking participants about their knowledge of smear tests, symptoms of cervical dysplasia, the meaning of smear tests, and what a colposcopy is.[31] They found that their questionnaire Cronbach’s alpha was .86. This suggests that this questionnaire may be more reliable. While the specific details of the questionnaire are unclear, we will design our own true/false questionnaire based off of the mentioned topics covered in this study. An example of this knowledge questionnaire can be seen in Appendix E.

To measure pain, prior studies have utilized the visual analog scale (VAS).[24,26-29,32] This scale is a self-reported tool that has been used extensively to study pain in various disciplines and has been well-validated.[40] Usually, it is a 10 cm line labeled with “no pain” on one end and “the worst pain I have ever felt” on the other end. Participants will then mark on the line the corresponding intensity of pain they felt. Reliability of the VAS for acute pain has also been found to be high with an intra-class correlation coefficient ranging from .97-.99 in patients with acute pain in the Emergency Department.[41,42] Moreover, it is applicable across a wide variety of populations and easy to administer. However, the VAS does have its limitations which include a ceiling effect and the inability to describe the quality of pain. In our proposed study, we are interested in the severity of pain and as such, these limitations are permissible.

Confounders

Previous studies indicate potential confounders consist of the following: age, smoking behavior, history of anxiety or depression, prior colposcopy, having multiple providers perform the colposcopy due to differences in patient interaction style, referring cytology severity, prior medical knowledge, parity, marital status, age, body mass index (BMI), educational level, waiting time, and procedure time. [3,25,29,30,32] Some of these confounders were selected based on the hypothesis that they (age, parity, and educational level) may be inversely related with anxiety as these patients may have more experience with medical exams and will therefore be more relaxed.[32] For BMI, it is hypothesized that those with a higher BMI may feel more ashamed during medical exams, thus influencing their anxiety levels during colposcopy.[32] Higher BMI may also make the exam more difficult, increasing the procedure time and in effect increasing anxiety levels. Other variables have been demonstrated to have an independent effect on anxiety. In the study conducted by Hilal et al., on multiple linear regression analysis, they found that study center (P=.028), smoking behavior (P=.025) and BMI (P= .033) had a significant effect on mean reduction of anxiety scores. [32] Another study examining predictors of pre-procedural anxiety found women who were single and women who had children independently predicted higher pre-colposcopy state anxiety ($p<0.05$).[3] The authors hypothesize that this may be due to a potential protective effect from having a partner in the case of being married and from fertility or family related concerns in the case of having children.[3] Finally, longer waiting times and longer procedures have been suggested in the literature as possible confounders as they may negatively influence anxiety although to date, no empirical studies have yet demonstrated this with data. [6,19,26,27,30,43]

Some studies also chose to record whether a biopsy or endocervical curettage (ECC) was performed during the exam as well as the mean number of biopsies taken.[24,26,29] In all three of the studies that recorded this data, none of these procedures were planned beforehand and patients were alerted to whether any of these procedures would be performed right before they were done. Chan et al. did not find that the performance of a biopsy during the procedure independently affected the anxiety levels of the participants while the other studies did not adjust for this variable in their data analysis. While the data so far has not demonstrated that the performance of a biopsy or ECC affects anxiety levels, it can be reasonably hypothesized that having these procedures performed during the colposcopic exam may influence anxiety levels as they may increase participants' worries about cancer. Consequently, it is reasonable to suggest that the performance of a biopsy or ECC during the exam may act as a potential confounder.

These potential confounders can ultimately be limited through appropriate exclusion criteria; the use of one clinician performing the colposcopic exam; recording baseline patient characteristics, waiting time and procedure time, and whether a biopsy or ECC was performed and how many; providing patients with an informational pamphlet concerning colposcopy and how to prepare for it; and through multivariate data analysis.

Selection Criteria

Most studies reviewed have included patients who were age >18, had the ability to read, write, or communicate in the native language of the country, and who had been referred for first time colposcopy.[10,26,29,31,32] The age criterion is based on data from previous studies that have found that cervical dysplasia is rarely found in women under the age of 20 and the average age of diagnosis of cervical cancer is 53, globally.[1,44] It is logical to limit the age of

participants to those >21 as this criterion will capture the target population, exclude adolescents who are not recommended to receive the Pap test, and simplify the protocol. The second criterion is another reasonable inclusion criterion as the intervention and the measures of anxiety all require the ability to communicate. In our proposed study, it will be reasonable to include English-speaking and Spanish-speaking patients to more fully capture our target population. Finally, the third criterion is justified as it has been hypothesized that previous experience with colposcopy may influence the anxiety levels of subsequent colposcopies.

Patients excluded in most of the reviewed studies included those who were blind, had a prior colposcopy, had mental impairments, or were currently pregnant. These exclusion criteria were chosen in consideration of practicalities of the intervention and to eliminate potential confounders.[15,18,24,27,32] Some prior studies have also chosen to exclude patients who have had a history of anxiety or depression but we will include these patients in our proposed study as we anticipate many of the people from our target population will have these disorders.[29,32] Moreover, we believe that including this patient population may help to guide care in decreasing anxiety in patients who need it the most.

Sampling Techniques

Virtually all reviewed studies have utilized consecutive sampling to achieve their sample size.[10,13,15,16,18-21,23,24,26-29,31,32] Consecutive sampling is a kind of nonprobability sampling technique, meaning that not every individual in the population has an equal likelihood of being selected for the study. However, due to the practical restraints of recruiting enough eligible patients, this will be an acceptable technique to recruit patients in our proposed study.

Intervention

Previous studies have utilized some model of video colposcope to allow the patients to view their own colposcopy exam as an intervention. One study reported that viewing the monitor was encouraged but the participants were not forced to do so.[23] Another study asked their participants to focused on the sensations they were feeling during the video colposcopy.[31] Most studies had more than one clinician performing the colposcopies with the exception of one study. Increased efficiency in the clinic is one advantage of having several clinicians perform colposcopies. However, having more than one clinician perform the colposcopy introduces the possible confounder of clinician style of interaction with patients. To limit confounders, it is justified in our study to limit all colposcopies to one clinician.

2.6 CONCLUSION

The existing literature on the efficacy of video colposcopy to decrease anxiety in first time colposcopy patients remains both scarce and inconclusive. Half of the randomized controlled trials suggest a potential benefit while the other half do not support this conclusion. Study design problems limit the interpretation of these results and provide insufficient evidence to either support or refute their conclusions. Moreover, limited generalizability due to the inadequate reporting of certain patient demographics of these studies leaves a gap in the literature about the effect of video colposcopy in low income patients who are disproportionately affected by this problem. As a simple interactive and educational tool that does not incur any known additional risks with colposcopy, video colposcopy represents a promising tool for further evaluation in patients presenting for first time colposcopy. A well designed prospective single blind randomized controlled trial will provide more robust data and help to bridge this gap as it will be the first study that will examine the effects of video colposcopy in reducing anxiety in a low-income racially diverse

patient population. Mean reduction of anxiety measured through the difference of pre-colposcopy STAI scores from post-colposcopy STAI scores will provide meaningful results on the effect of video colposcopy on anxiety while patient adherence to follow-up, patient knowledge of colposcopy and cervical dysplasia, patient satisfaction, and patient pain during the procedure as secondary outcomes will provide meaningful data on other potential benefits of video colposcopy.

2.7 REFERENCES

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Chapter 3: Study Methods

3.1- STUDY DESIGN

We will conduct a prospective single blind randomized controlled trial in low-income women referred to the Yale New Haven Hospital Women's Center for first time colposcopy. Patients will be randomized to the intervention group or the control group using a computerized randomization tool. To implement a single blind design, we will inform patients that we are conducting a study on anxiety but will not inform them about the role of video colposcopy until the colposcopic exam is over. This will decrease performance bias. Due to the nature of the intervention, the clinician performing the colposcopy will not be blinded. Data analysts will be blinded to further decrease bias.

3.2-STUDY POPULATION AND SAMPLING

Our study population will include women presenting to Yale New Haven Hospital's Women's Center (a U.S. safety net clinic serving a racially and ethnically diverse population of low-income women) for first cervical colposcopy. All patients who satisfy the inclusion and exclusion criteria will be eligible for the study and will be approached to participate in the study. We will use consecutive sampling to recruit patients until we have satisfied our calculated sample size of 286 patients total with 143 patients in each arm.

Inclusion Criteria

Our inclusion criteria will include the following: ability to read, write or communicate in English or Spanish, age >21, Medicaid or uninsured insurance status, and referral for first time colposcopy. English and Spanish speakers will be included in this study as these are the most predominantly spoken languages in New Haven, CT. Those falling outside of these languages will be excluded to simplify the protocol but ensure that most of the population presenting to the

Women's Center are able to participate in the study. Women over the age of 21 will be included to further simplify the protocol and exclude adolescents. Medicaid or uninsured insurance status will serve as a proxy for low-income individuals.

Exclusion Criteria

Our exclusion criteria will include the following: presence of a language barrier, mental impairment, inability to provide informed consent, blindness, prior colposcopy, or current pregnancy. These exclusion criteria will be used due to the practical limitations of the intervention and to decrease the number of potential confounders.

3.3-SUBJECT PROTECTION AND CONFIDENTIALITY

We will obtain Institutional Review Board (IRB) approval as dictated by the Yale IRB Policy 100 PR.1 Review by a Convened Institutional Review Board. For every eligible participant, we will require written, informed consent. As outlined in the Yale IRB policy 200 Informed Consent for Human Research form, informed consent will be conducted in a clear and understandable manner to the participant. The consent form will outline the purpose of the study, the duration of participation, description of the procedures, and possible risks or discomforts. Possible benefits that can be reasonably expected as a result from the research will be relayed to the patient as well as any disclosures of any appropriate alternative procedures, if any, that may be beneficial to the participants. The consent form will further include confidentiality practices, investigator contact information should any questions or concerns arise, and a statement that research participation is completely voluntary and that the participant may discontinue participation at any time with no penalty. A signed copy will be given to the participant for personal records. An example consent form is shown in Appendix A.

All staff members involved in the study will be required to successfully complete Health Insurance Portability and Accountability Act (HIPAA) training prior to the start of the study and carry out study protocols in accordance with HIPAA regulations. The research assistant will explain to participants their HIPAA rights and participants will also receive a brochure containing detailed information about HIPAA prior to signing the informed consent form.

The medical information collected throughout the duration of the study will be stored on a secure server with data encryption software. Access to this information will be restricted to the research team members directly involved in the study and will be password protected. Participant identifiers like name, date of birth, and medical record number will be replaced as soon as possible by a random computer-generated identification number to maintain participant privacy.

3.4-RECRUITMENT

Patients referred to the Yale New Haven Hospital's Women's Center will be screened to participate in the study. Those who fulfill the inclusion and exclusion criteria will be eligible for the study. The research assistant will approach study participants during the initial consultation and inform them of the medical implications of the study. They will be informed that participating in the study is completely voluntary and that if they do decide to participate, informed consent will need to be obtained. Participants will not be compensated for participation in this study.

3.5-STUDY VARIABLES AND MEASURES

We will utilize video colposcopy as the intervention and the model of video colposcope we will use will be the Cooper Surgical Leisegang Optik Model 2 video colposcope. This model is a photo swing colposcope with a Canon EOS Rebel Camera that has high quality German optics. During the colposcopy, patients will be able to view a television monitor that transmits a

real time feed of the exam and participants will be encouraged to participate in their own care. Colposcopic findings will be discussed with the participant during the exam. The control will be a traditional non-video colposcopy. The patient will be unable to view her colposcopy if assigned the control group and colposcopy findings will be discussed with the participant after the exam has concluded. The primary outcome variable will be the reduction of anxiety as measured by the difference of pre-colposcopy and post-colposcopy STAI. An example of the STAI questionnaire we will use is shown in Appendix C. Secondary outcome variables will include patient adherence to follow-up, patient satisfaction, patient knowledge of colposcopy and cervical dysplasia, and patient pain during the procedure. Adherence to follow-up will be measured by whether or not the patient returns for the follow-up appointment or reschedules the original appointment. Patient satisfaction will be measured by the Patient's Experience and Attitude Colposcopy Eindhoven Questionnaire (PEACE-q). An example of this questionnaire can be seen in Appendix D. Patient knowledge of colposcopy and cervical dysplasia will be measured by a post-colposcopy true/false questionnaire. A correct answer will equal 1 point while an incorrect answer will equal 0 points. A higher total score will correspond with better knowledge about cervical dysplasia and colposcopy. An example of this questionnaire can be seen in Appendix E. Patient pain during the procedure will be measure with the VAS. An example of the VAS we will use is shown in Appendix F.

3.6-METHODOLOGY CONSIDERATIONS

Blinding

The participants will be blinded to the intervention. We will ask eligible patients to participate in a study about reducing anxiety but we will not inform the patients about the role of video colposcopy until after the exam. Due to the nature of the study, the colposcopist will not be

blinded. Outcome assessors and data analysts will be blinded to which group participants were randomized, in order to decrease information bias.

Assignment of Intervention

Patients will be assigned to treatment or control groups through a computerized randomization tool by a nurse not directly involved with the study. These allocation lists will then be placed into opaque envelopes to be opened right before the colposcopy. Participants will be allocated in a 1:1 ratio.

Monitoring of Adverse Events

At follow-up, study participants will be asked if they had experienced any complications as a result of the colposcopy including: bleeding, abdominal or pelvic pain, vaginal discharge, or signs of infection like fever. Should any of these patients experience any concerning symptoms in the days following colposcopy, they will be informed to call the clinic and be evaluated. If a patient fails to show up for their follow-up appointment, patients will be called over the phone to reschedule their original appointment and asked about any of these complications.

Data Collection

The women who agree to participate in the study and give informed consent will fill out either the English or the Spanish version of the STAI questionnaire as well as baseline patient demographics prior to the colposcopic exam. Immediately after the colposcopy, patients will fill out another questionnaire containing only the state version of the STAI, the true/false patient questionnaire, PEACE-q questionnaire, and the VAS. Data on participant adherence to follow-up will be collected as follows: those who attend their follow-up appointment or reschedule will be recorded as adherent while whose fail to do either of those will be considered non-adherent.

Sample Size Calculation

Our sample size calculation is based on data from Danhauer et al. who has a similar patient population to our target population and Chan et al. who found music to decrease anxiety in first time colposcopy patients.[1,2] In the study by Danhauer et al., the mean change in STAI with traditional colposcopy was 2.6. In the study conducted in 2003 by Chan et al. a mean change in STAI of 7.11(SD of 12.84) was found in the music group. Assuming that this intervention will have a similar or non-inferior effect, 7.11-2.6=4.5 which will be the estimated effect size. Thus, a sample size of 256 will be required to detect an effect size of 4.5 with an α of 5% and a power of 80%. Assuming a 10% drop out rate and to ensure an even number of participants in each arm, a conservative sample size of 286 will be required with 143 in each arm. The sample size calculation is included in Appendix B.

Data Analysis

Descriptive statistics will include age, BMI, smoking behavior, race/ethnicity, SES bracket, educational level, parity, marital status, referring cytology, and current concomitant disease. They will be reported as means and standard deviation for parametric data or as medians and interquartile range for non-parametric data. Categorical data will be reported as relative frequencies. The primary outcome will be mean reduction in STAI and will be reported as means and standard deviation. Correspondingly, we will use a t test for the statistical analysis. The secondary outcomes will be adherence to follow-up, patient satisfaction, patient knowledge, and pain during the procedure. Patient adherence to follow-up will be reported as proportions. We will use the Chi Square test for statistical analysis. Patient satisfaction will be measured with the PEACE-q and will be reported as means and standard deviation. Accordingly, we will use the t test for statistical analysis. Patient knowledge will be assessed using a true/false questionnaire. A correct answer will earn 1 point while an incorrect answer will earn 0 points. The sum will be

reported as means and standard deviation. Correspondingly, we will utilize a t test for statistical analysis. Finally, we will measure pain during the procedure using VAS and it will be reported as means and standard deviation. For statistical analysis we will use the t test for statistical analysis. A significance of $P < 0.05$ will be considered achieving statistical significance and all statistical tests will be two-tailed. Analysis will be done under the intention to treat principle. To account for the effect of potential confounders, multiple linear regression will be performed with the reduction in STAI scores as the dependent variable and study group, age, BMI, smoking behavior, race, SES, marital status, waiting time, procedure time, performance of a biopsy or ECC, and level of education as independent variables. Baseline characteristics of all participants will be obtained at the initial consultation. An example of these characteristics can be seen below in Table 1.

Table 1: Participant Baseline Characteristics

	Video Colposcopy N=143	Control N=143	P-Value
Age (years)	Mean ±SD	Mean ±SD	T test
Income (USD)			Chi square
<$20,000	(n)%	(n)%	
>$20,000	(n)%	(n)%	
Marital Status			Chi square
Single	(n)%	(n)%	
Divorced	(n)%	(n)%	
Widowed	(n)%	(n)%	
Married	(n)%	(n)%	
Cohabitated	(n)%	(n)%	
Highest level of education achieved			Chi square
None	(n)%	(n)%	
High School	(n)%	(n)%	
Associate's Degree	(n)%	(n)%	
Bachelor's Degree	(n)%	(n)%	
Master's Degree	(n)%	(n)%	
PhD	(n)%	(n)%	
Race			Chi square
White	(n)%	(n)%	
Hispanic	(n)%	(n)%	

Asian Black Other	(n)% (n)% (n)%	(n)% (n)% (n)%	
Referring Pap test ASCUS AGC LSIL HSIL Other	 (n)% (n)% (n)% (n)% (n)%	 (n)% (n)% (n)% (n)% (n)%	Chi square
Parity Nulliparity Primiparity Multiparity	 (n)% (n)% (n)%	 (n)% (n)% (n)%	Chi square
Body Mass Index ($kg/m^{2)}$	Median/ IQ range	Median/ IQ range	Whitney U
Waiting time in waiting room (minutes)	Mean ±SD	Mean ±SD	T-test
Colposcopy procedure time (minutes)	Mean ±SD	Mean ±SD	T-test
Current smoker	(n)%	(n)%	Chi square
History of anxiety or depression	(n)%	(n)%	Chi square
Current use of any SSRIs or benzodiazepines	(n)%	(n)%	Chi square
Current concomitant disease (yes/no)*	(n)%	(n)%	Chi square
Colposcopic impression Normal CIN 1 CIN 2/3 Suspicious for invasion Nonspecific	 (n)% (n)% (n)% (n)% (n)%	 (n)% (n)% (n)% (n)% (n)%	Chi square
Performance of procedure Biopsy (yes/no) ECC (yes/no) No	 (n)% (n)% (n)%	 (n)% (n)% (n)%	Chi square
Number of biopsies taken	Mean ±SD	Mean ±SD	T-test

*Current concomitant disease will be recorded via patient self-report and will constitute an answer of yes if patient is currently being evaluated or treated for any medical conditions

3.6- TIMELINE AND RESOURCES

Our study will be performed over a two-year time period. This time frame includes recruitment, data collection, and statistical analysis. Currently, the Yale New Haven Hospital Women's Center schedules about twenty colposcopies or loop electrosurgery excision surgeries

(LEEPs) every week. Based on this data and our consecutive sampling method, we will conservatively estimate that it will take approximately 6 months to recruit the necessary number of eligible patients accounting for both patients who choose not to participate in the study and a 10% dropout rate. Data collection will occur simultaneously and follow-up will take up to a maximum of one year. We expect data analysis to take 1-3 months.

Our study will require one principle investigator, one co-principle investigator, one gynecologist trained in colposcopy, one colposcopy clinic nurse, and one Spanish speaking research assistant. The research assistant will help with recruitment and serve as a resource for participants to ask any questions should they have any when approached for the study. The colposcopy nurse will help carry out the protocols and oversee patients while they are filling out their questionnaires. The gynecologist trained in colposcopy will perform all colposcopies regardless of which group participants were randomized, in order to limit the confounding effects of having multiple providers perform the colposcopic exam. The principle investigator and co-principle investigator will oversee the study as a whole to ensure protocols are being carried out appropriately. The co-principle investigator and research assistant will perform the data analysis.

3.7-REFERENCES

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Chapter 4: Conclusion

4.1 -ADVANTAGES AND DISADVANTAGES

This proposed study serves to synthesize existing literature to provide more robust evidence on the efficacy of video colposcopy to reduce anxiety in a patient population that has yet to be studied. One key advantage of this study over previous studies is the utilization of design protocols intended to minimize bias. Previous studies on video colposcopy have been unblinded due to the nature of the intervention. [1-4] Our study has the advantage of a single blind design to decrease performance and ascertainment bias. Next, the use of a single provider to perform the colposcopy and adjusting for several important confounders in the data analysis increases the likelihood that we are assessing the true relationship between video colposcopy and anxiety. As a result, these design elements will produce more robust and accurate results. Our secondary outcome of patient adherence to follow-up may also provide more evidence in the existing literature about improving patient adherence with a larger sample size.[5] Finally, a major advantage our study has compared to the existing literature is the new data that will be obtained regarding anxiety reduction with video colposcopy in low-income patients. Overall, the proposed study will provide more compelling evidence on the efficacy of video colposcopy to decrease anxiety, in a population previously unstudied.

Disadvantages of our study include not being able to blind the gynecologist performing the colposcopies, the limited external validity of the study, and the use of a self-reported measure of anxiety. While we will be blinding participants to the intervention, we will be unable to blind the gynecologist who will perform the colposcopies due to the nature of the intervention. This introduces a source of performance and ascertainment bias. Studying low-income patients also limits our external validity. Nevertheless, as there is currently no data evaluating video

colposcopy's effect on anxiety in this population and considering that they are the most negatively affected by cervical cancer, the results of this study will contribute important and meaningful data to the existing literature. Finally, as we have chosen to use STAI as our measure of anxiety and it is a self-reported index of anxiety, we will only have subjective data and no objective measure of anxiety. However, as STAI has been the gold standard to measure anxiety across various disciplines, we believe that this limitation is acceptable.

4.2-CLINICAL AND/OR PUBLIC HEALTH SIGNIFICANCE

Routine cervical cancer screening is the pillar of prevention that has helped decrease the incidence and prevalence rate of cervical cancer in the U.S. since the 1950's. However, recent data indicates that these trends are stagnating indicating the need for improvements in management and screening.[6] Studies examining predictors of poor screening indicate that anxiety is a significant barrier.[7,8] A wealth of studies examining interventions to decrease this barrier exist in the current literature but no single intervention has demonstrated consistent results. A few previous studies have explored the effect of using video colposcopy to reduce anxiety in first time colposcopy patients but these studies have design shortcomings and have produced mixed results. Furthermore, the results of current literature remain limited to certain populations. The lack of reporting of certain demographic data from previous studies leaves the effect of video colposcopy on anxiety in low income patients unknown and an area of significant interest.

Results from this study will provide novel and quality data on whether video colposcopy has any utility in decreasing anxiety in low-income patients. This may in turn establish video colposcopy as a simple and easily employed tool for colposcopy clinics to decrease anxiety to improve cervical cancer screening. If this study finds a negative result, the results will still

provide meaningful data to guide future directions in finding a useful intervention to decrease anxiety in low-income women presenting for first time colposcopy.

4.3-REFERENCES

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Appendix A: Consent Forms

CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL WOMEN'S CENTER

Study Title: VIDEO COLPOSCOPY FOR DECREASING ANXIETY IN A LOW-INCOME SETTING
Principal Investigator: Sangini Sheth, MD, MPH
Co-Principal Investigator: Jessica Zheng, PA-SII
Funding Source: Yale University School of Medicine Physician Associate Program

Invitation to Participate and Description of Project:

You are invited to participate in a research study about interventions to reduce anxiety in first time colposcopy patients. You have been asked to participate because you are over the age of 21 and have been referred for colposcopy for the first time following an abnormal Pap test result. Approximately 286 patients will participate in this study.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the research study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form. You will receive a copy of this signed form for your records.

Description of Procedures:

- If you decide to participate in this study, you will be randomly assigned to one of two groups. The first group will undergo colposcopy with the intervention and the second group will undergo a traditional colposcopy. Randomization will be achieved with a random computer-generated sequence.
- Prior to undergoing your colposcopy, you will be asked to fill out some demographic information as well as some questionnaires regarding your level of anxiety. We ask that you complete these questionnaires to the best of your ability.
- Following your colposcopy, you will be asked to complete a couple of questionnaires about anxiety, pain, your knowledge of cervical cancer/colposcopy, and your overall colposcopy experience.
- Depending on which group you have been randomized to, the provider performing the colposcopy will inform you of the findings during the exam or after. The same provider will perform all colposcopies in the study.
- After the colposcopy, you will be asked to set up a follow-up appointment to monitor for any changes. Once you have attended your follow-up appointment, that will mark the

end of your enrollment of this study. We anticipate the total enrollment time of this study to be a maximum length of 12 months but depending on your findings, the enrollment time may be shorter.

- You will be alerted of any important or significant findings that are discovered during the course of your participation in this study that may affect your willingness to continue your participation. If we find that one method offers better outcomes than the other, we will conclude the study and offer the better method to all of our participants.
- You may voluntarily withdraw from this study at any time.
- A description of this clinical trial will be available on http://www.Clinicaltrials.gov as required by U.S. Law. This website will not include any information that will personally identify you. The purpose of this database is to allow everyone to see what research has been done and what research is currently being done. At most, the website will include summary of the results. You can search this website at any time. If research results are published, your personal information will not be given.

Risks and/or Inconveniences:

- Colposcopy can be an uncomfortable and anxiety provoking procedure for many patients. We will do our best to maintain an environment that is as comfortable as possible within our means.
- The risks of colposcopy include some pain or discomfort during and after the procedure. A previous study found that around 14-18% of women experienced one of these symptoms after colposcopy. Extremely rare complications of colposcopy include severe abdominal or pelvic pain, heavy bleeding lasting longer than two weeks, purulent vaginal discharge, fever or chills, and infection. Should any of these symptoms arise following the procedure, you should contact the clinic to be evaluated and treated. Colposcopy will not make it more difficult to become pregnant.
- Biopsies or endocervical curettage may need to be performed during the colposcopy depending on the colposcopy findings. Rare complications of these procedures include bleeding or infection of the site. Should there be any significant bleeding we will apply ferric subsulfate (Monsel's solution) with a cotton swab to the area. Signs of infection may present as pelvic pain, purulent vaginal discharge, or abnormal bleeding or clotting. If any of these signs or symptoms are present after the procedure, you should contact the clinic to be evaluated and treated for possible infection.
- The intervention being studied has reported no additional major risks or side effects compared to standard traditional colposcopy.

Benefits

- This research may provide more conclusive evidence on methods to decrease anxiety in low income patient populations presenting for first time colposcopy.
- This study may improve current colposcopy practice and potentially increase cervical cancer screening rates.
- We expect this study to directly benefit low income populations and indirectly benefit other populations of patients undergoing colposcopy.

Economic Considerations

There will be no compensation for participation in this study and no costs will be associated with your participation in the study. Parking will be provided free of charge.

Treatment Alternatives

If you choose not to participate in this study, you may proceed with a traditional colposcopy. Other strategies used to decrease anxiety in first time colposcopy patients include informational pamphlets, video information, counselling sessions, guided imagery, targeted information, and music. You will be given an informational pamphlet at the initial consultation but other strategies will not be used in this study.

Confidentiality

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as required by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. Information will be kept confidential by replacing personal identifiers with identification numbers on study forms, storing signed forms in locked cabinets, and storing collected data on a password protected, HIPAA compliant, encrypted server. When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific permission is obtained.

We understand that information about your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will collect information that identifies you personally. This may include your name and address, telephone number, and email address, or mobile phone number. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The data will be kept in this form until 2 weeks after acquisition of all study data, at which the personal information will be destroyed and the data will become anonymous. The data will remain in this anonymous form indefinitely.

The information about your health that will be collected in this study includes:

- Records about past medical history
- Records about phone calls made as part of this research study
- Records about your study visits

Information about you and your health that might identify you may be used by or given to:

- Representatives from Yale University, the Yale Human Research Protection Program and the Yale Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.

- Those individuals at Yale who are responsible for the financial oversight of research including billings and payments
- The Principal Investigator (Dr. Sangini Sheth)
- Co-Investigators and other investigators
- Study Coordinator and Members of the research team

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine are required to comply with HIPAA and to ensure the confidentiality of your child's information.

If you choose to participate in this study, the investigators will check your electronic medical record at Yale (EPIC) to make sure you qualify. Any access to your electronic medical record will be done consistent with HIPAA regulations.

Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies. This authorization to use and disclose your health information collected during your participation in this study will never expire.

In Case of Injury

If you are injured while participating in the study, seek treatment and contact the study doctor as soon as you are able.

Yale School of Medicine and Yale-New Haven Hospital do not provide funds for the treatment of research-related injury. If you are injured as a result of your participation in this study, treatment will be provided. No additional financial compensation for injury or lost wages is available. You do no give up any of your legal rights by signing this form.

Voluntary Participation and Withdrawal

Subjects have the right to withdraw their data once it has been collected. However, this will only be possible before it has been deidentified. Once data has been collected and deidentified, subjects will not be able to withdraw their data.

Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study or receive study procedures as a study participant if you do now allow us to use your information as part of this study. You do not give up any of your legal rights by signing this form.

Withdrawing from the Study

If you do not become a subject, you are free to stop and withdraw from this study at any time during its course. To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. This will cancel any future appointments.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors or with Yale-New Haven Hospital or Yale University.

When you withdraw from the study, no new health information identifying you will be collected after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to ensure the integrity of the study and/or study oversight.

Questions

We have used some technical terms in this form. Please feel free to ask about anything you do not understand and to consider this research and the consent form carefully- as long as you feel necessary- before you make a decision.

Authorization

I have read (or someone has read to me) this form and have decided to continue to participate in the project described above. Its general purposes, the particulars of involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

Name of Subject:_____

Signature:_____

Date:_____

_____ _____

Signature of Principal Investigator Date

or

_____ _____

Signature of Person Obtaining Consent Date

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator *Sangini Sheth MD,MPH at (***)***-**** or the Co-Principal Investigator Jessica Zheng at (***)***-****.* If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions, offer input, discuss situations in the event that a member of the research team is not available, or if you have any questions concerning your rights as a research subject, you may contact the Human Investigation Committee at (203) 785-4688.

SHORT FORM WRITTEN CONSENT

FOR SUBJECTS WHO ARE UNABLE TO READ ENGLISH

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL WOMEN'S CENTER

Study Title: VIDEO COLPOSCOPY FOR DECREASING ANXIETY IN A LOW-INCOME SETTING
Principal Investigator: Sangini Sheth, MD, MPH
Co-Principal Investigator: Jessica Zheng, PA-SII
Funding Source: Yale University School of Medicine Physician Associate Program

CONSENT TO PARTICIPATE IN RESEARCH

You are being asked to participate in a research study.

Before you agree, the investigator must tell you about the (i) purposes, procedures, and duration of the research; (ii) any procedures which are experimental; (iii) any reasonably foreseeable risks, discomforts, and benefits of the research; (iv) any potentially beneficial alternative procedures or treatments; and (v) how confidentiality will be maintained.

Where applicable, the investigator must also tell you about (i) any available compensation or medical treatment if injury occurs; (ii) the possibility of unforeseeable risks; (iii) circumstances when the investigator may halt your participation; (iv) any added costs to you; (v) what happens if you decide to stop participating; (vi) when you will be told about new findings which may affect your willingness to participate; and (vii) how many people will be in the study.

If you agree to participate, you must be given a signed copy of this document and a written summary of the research.

You may contact either the Principal Investigator Dr. Sangini Sheth at (***)***-**** or the Co-principal investigator Jessica Zheng at (***)***-**** any time you have any questions about the research or what to do if you are injured. You may contact the Yale Human Research Protection Program (HRPP) at (203)785-4688 if you have any questions about your rights as a research subject.

Your participation in this research is voluntary and you will not be penalized or lose benefits if you refuse to participate or decide to stop.

Signing this document means that the research study, including the above information, has been described to you orally, and that you voluntarily agree to participate.

_____ _____

Signature of Participant/LAR Date

_____ _____

Signature of Witness Date
(This should not be the person obtaining consent)

Witness/Interpreter

By signing this form, you are indicating that:

- The information in the summary document as well as any additional information conveyed by the research person obtaining consent was presented to the subject in a language preferred by and understandable to the subject
- The subject's questions were interpreted and the response of the person obtaining consent were presented in a language preferred by and understandable to the subject
- At the conclusion of the consent conference the subject was asked in a language preferred by and understandable to the subject if s/he understood the information and responded affirmatively.

_____ _____

Signature of Witness/ Interpreter Date

SPANISH SHORT FORM WRITTEN CONSENT

FORMULARIO ABREVIADO DE CONSENTIMIENTO ESCRITO

PARA INDIVIDOS QUE NO HABLAN NI LEEN EL INGLÉS

ESCUELA DE MEDICINA DE LA UNIVERSIDAD DE YALE-HOSPITAL YALE-NEW HAVEN CENTRO DE MUJERES

Nombre del estudio: VIDEO COLPOSCOPIA PARA DISMINUIR LA ANSIEDAD EN UNA CLÍNICA DE BAJOS INGRESOS
Investigador principal: Sangini Sheth, MD, MPH
Investigadora codirectora: Jessica Zheng, PA-SII
Fuente de financiamiento: Escuela de medicina de la Universidad de Yale Programa de medico asociado

CONSENTIMIENTO PARA PARTICIPAR EN LA INVESTIGACIÓN

Se le está solicitando su participación en un estudio de investigación.

Antes de aceptar, el investigador debe informarle sobre: (i) los propósitos, los procedimientos, y la duración del estudio; (ii) todo los procedimiento que seas experimentales; (iii) todos posibles riesgos, incomodidad o beneficio que se puede prever como resultado del estudio; (iv) cualquier procedimiento o tratamiento alternativo que tenga potencial de beneficiarle; y (v) cómo se mantendrá la confidencialidad.

Cuando sea aplicable, el investigador también debe informarle sobre: (i) cualquier compensación o atención médica disponible en caso de lesion; (ii) la posibilidad de riesgos impredecibles; (iii) situaciones en las que el investigador pueda cesar su participación; (iv) cualquier costo adicional para usted; (v) lo que pasa si usted decide interrumpir su participación; (vi) cuándo se le informará sobre nuevos hallazgos que puedan afectar su deseo en participar; (vii) cuántas personas participarán en el estudio; y su derecho de revocar (anular) su autorización para el uso o la divulgación de sus datos de salud confidenciales por parte de los investigadores.

Si usted acepta participar, debe recibir una copia firmada de este documento y un resumen del estudio por escrito.

Puede comunicarse con La Doctora Sangini Seth al (***)***-**** o con Jessica Zheng al (***)***-**** a qualquier momento que tenga preguntas sobre el estudio o lo que debe hacer si se encuentra herido. Puede comunicarse con el Programa de Protección de Investigación Humana de Yale (HRPP) al (203)785-4688 si tiene preguntas sobre sus derechos como sujeto de una investigación.

Su participación en esta investigación es voluntaria, y usted no será penalizado ni perderá beneficios al negar su participación o al optar por interrumpirla.

Al firmar este documento, usted consenta que el estudio de investigación, incluyendo la información previa, le ha sido explicado oralmente, y que usted acepta participar voluntariamente.

_____ _____
Firma del participante/LAR Fecha

_____ _____
Firma del testigo Fecha
(No debe ser la misma persona obteniendo el consentimiento)

Testigo/ Intérprete

Al firmar este formulario, usted afirma que:

- La información en el Documento Sumario (el formulario abreviado) y toda la información adicional comunicada por el investigador obteniendo el consentimiento del sujeto, se presentó al sujeto en su idioma preferido y de manera comprensible.
- Las preguntas del sujeto fueron interpretadas y las respuestas de la persona obteniendo el consentimiento fueron transmitidas al sujeto en su idioma preferido y de la manera comprensible.
- Al cierre de la conferencia de consentimiento, se le preguntó al sujeto en su idioma preferido y de manera comprensible, si había comprendido toda la información y respondía afirmativamente.

_____ _____
Firma del testigo/intérprete Fecha

Appendix B: Sample Size Calculation

The sample size calculation was based on a t-test calculator comparing two independent means assuming normal distribution with the following study parameters:

- Alpha, the probability of a type-I error (finding a difference when a difference does not exist): 0.05
- Beta, the probability of a type-II error (not detecting a difference when one actually exists: 0.2
- Power: 0.8

The following equation was used to calculate the sample size:

$$k = \frac{n_2}{n_1} = 1$$

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2/K)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

$$n_1 = \frac{(12.84^2 + 12.84^2/1)(1.96 + 0.84)^2}{4.5^2}$$

$$n_1 = 128$$

$$n_2 = K * n_1 = 128$$

Assuming a standard deviation of 12.84 units, the study would require a sample size of 128 for each group (total sample size of 256) to achieve a power of 80% and a level of significance of 5% (two sided), for detecting a true difference in means between the test and the reference group of 4.5.

Assuming a 10% drop out rate and to ensure an even number of participants in each arm, a final conservative sample size of 286 will be required with 143 in each arm.

Reference: Dhand, N. K., & Khatkar, M. S. (2014). Statulator: An online statistical calculator. Sample Size Calculator for Comparing Two Independent Means. Accessed 15 December 2019 at http://statulator.com/SampleSize/ss2M.html

Appendix C: STAI Questionnaire

Name_____Date_____Age_____

Directions: A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate value to the right of the statement to indicate how you feel **right now**. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your **present feelings** best.

	Almost never	Sometimes	Often	Almost Always
1. I feel calm.	0	1	2	3
2. I feel secure.	0	1	2	3
3. I am tense.	0	1	2	3
4. I feel strained.	0	1	2	3
5. I feel at ease.	0	1	2	3
6. I feel upset.	0	1	2	3
7. I am presently worrying over possible misfortunes.	0	1	2	3
8. I feel satisfied.	0	1	2	3
9. I feel frightened.	0	1	2	3
10. I feel comfortable.	0	1	2	3
11. I feel self-confident.	0	1	2	3
12. I feel nervous.	0	1	2	3
13. I am jittery.	0	1	2	3
14. I feel indecisive.	0	1	2	3
15. I am relaxed.	0	1	2	3
16. I am content.	0	1	2	3
17. I am worried.	0	1	2	3
18. I feel confused.	0	1	2	3
19. I feel steady.	0	1	2	3
20. I feel pleasant.	0	1	2	3

Directions: A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate value to the right of the statement to indicate how you **generally** feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you **generally** feel.

	Almost never	Sometimes	Often	Almost Always
21. I feel pleasant.	0	1	2	3
22. I feel nervous and restless.	0	1	2	3
23. I feel satisfied with myself.	0	1	2	3
24. I wish I could be as happy as others seem to be.	0	1	2	3
25. I feel like a failure.	0	1	2	3
26. I feel rested	0	1	2	3
27. I am "calm, cool, and collected"	0	1	2	3
28. I feel that difficulties are piling up so that I cannot overcome them.	0	1	2	3
29. I worry too much over something that really does not matter.	0	1	2	3
30. I am happy.	0	1	2	3
31. I have disturbing thoughts.	0	1	2	3
32. I lack self-confidence.	0	1	2	3
33. I feel secure.	0	1	2	3
34. I make decision easily.	0	1	2	3
35. I feel inadequate.	0	1	2	3
36. I am content.	0	1	2	3
37. Some unimportant thoughts run through my mind and bothers me.	0	1	2	3
38. I take disappointments so keenly that I can't put them out of my mind.	0	1	2	3
39. I am a steady person.	0	1	2	3
40. I get in a state of tension or turmoil as I think over my recent concerns and interests.	0	1	2	3

Reference: Spielberger CD, Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1970.

Appendix D: PEACE-q Questionnaire

PATIENT'S EXPERIENCE AND ATTITUDE COLPOSCOPY EINDHOVEN QUESTIONNAIRE (PEACE-Q)

Directions: A number of statements about your experience with colposcopy are given below. Read each statement and then circle the appropriate value to the right of the statement to indicate how strongly you agree or disagree with the statement. There are no right or wrong answers but give the answer which corresponds best with your experience with colposcopy.

	Strongly agree	Agree	Disagree	Strongly disagree
1. I was well-informed about the colposcopy.	1	2	3	4
2. I was preoccupied with the possible outcome of the colposcopy.	1	2	3	4
3. I feel stressed about the colposcopy.	1	2	3	4
4. I was worried about the outcome of the colposcopy.	1	2	3	4
5. I was worried about the possible further treatment options.	1	2	3	4
6. The gynecologist put me at east.	1	2	3	4
7. I am satisfied about the way I received the results.	1	2	3	4
8. I was well-informed about the next steps after the colposcopy.	1	2	3	4

Reference: Pop VJM, Wouters T, Bekkers RLM, Spek VRM, Piek JMJ. Development of the Patient's Experience and Attitude Colposcopy Eindhoven Questionnaire (PEACE-q). BMC Health Services Research. 2019;19(1):589.

Appendix E: True/False Questionnaire

Directions: Below is a true/false questionnaire about colposcopy and cervical dysplasia. Circle either True or False. Please answer to the best of your ability.

1. True / False An abnormal Pap test means that I definitely have cancer.
2. True / False If abnormal cells are found during my colposcopy, a biopsy will be done.
3. True / False Cervical dysplasia is another term for cancer.
4. True / False HPV infection is a risk factor for the development of cervical dysplasia.
5. True / False A Pap test is a test to detect pre-cancer and cancer.
6. True / False There are usually no symptoms when a person has cervical dysplasia.
7. True / False Colposcopy is a procedure used to examine my cervix after an abnormal Pap test result.

Appendix F: Visual Analog Scale

Directions: Please mark with a vertical line through the horizontal line below to indicate your response to the question.

Question: How painful was the colposcopy exam?

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