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Cancer Salient Messaging for Human Papillomavirus (HPV) Vaccine Uptake: A Randomized Controlled Trial

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2013

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An abstract of
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Abstract

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Introduction: Routine vaccination with the HPV vaccine is recommended for adolescents aged 11-12 years old, but uptake is suboptimal. Parents and providers are often uncomfortable discussing sexual practices of their adolescents, which have contributed to the delay or refusal of the HPV vaccine for the target age group. We created a cervical cancer salient message to promote HPV vaccination, by emphasizing disease salience and disease threat, while promoting self-efficacy. This trial tested the effects of a cervical cancer salient message on vaccine confidence and intent to vaccinate when compared to an infection salient message from the CDC and non-vaccine control.

Methods: A 3-arm randomized trial was conducted. Parents of adolescent girls (aged 9-17) were eligible for the study. Participants' vaccine confidence and intent to vaccinate were measured at baseline, and post intervention message. Surveys were administered online through Amazon Mechanical Turk.

Results: 14,165 people were screened, 1,084 participants were eligible for the follow-up survey with 653 people were counted in our final sample, yielding a 60.2% response rate. Parents who received the cervical cancer message or the CDC message were no more likely to report intent to vaccinate against HPV, and no more confident in vaccines than participants who received the non-vaccine control message.

Conclusions: Neither message had an overall effect on intent to vaccinate, highlighting the need for more research in this field to identify successful messaging strategies for HPV. Exploratory analyses suggest that among parents with 'Low' vaccine confidence at baseline, the cervical cancer framed message may be more effective in changing intention than the CDC message or the non-vaccine related control. This finding suggests future work should target groups with 'Low' or 'Medium' vaccine confidence at baseline as they may be more amenable to change, and more receptive to disease salient messaging.

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Chapter I: Background

Human Papillomavirus (HPV) is the most common sexually transmitted infection in the United States, with almost 14 million people becoming infected each year between the ages of 15-59 (1). Of those, nearly half of all new infections are occurring among 15-24 year olds (2). There have been roughly 150 strains of HPV identified, with nearly 40 strains attacking the genital area (3). Most HPV infections are asymptomatic and clear on their own within 2 years, but persistent infections can lead to diseases, including several cancers and genital warts. There is currently no treatment for an HPV infection (1, 4).

Cervical cancer is the most common cancer caused by HPV infection, and virtually all cervical cancers can be attributed to HPV infection. Based on their epidemiologic association to cervical cancer, HPV strains are classified as either low- or high- risk. High-risk types can cause low-grade cervical cell abnormalities, high-grade cervical cell abnormalities, and cancers (5). Despite the many strains, HPV types 16 and 18, both classified as high-risk, account for nearly 70% of all cervical cancers (1). Each year about 12,000 new cases of invasive cervical cancer are diagnosed, and about 4,000 women die from the disease (6). While cervical cancer is the most common cancer caused by HPV infection, HPV can also lead to cancer of the vulva, vagina, penis, anus and oropharynx (4). In total, roughly 27,000 people get cancer caused by a persistent HPV infection yearly in the United States (4).

There is no cure for HPV, but HPV can be prevented through vaccination. The first HPV vaccine came to market in 2006, and since then there have been a series of

shifting recommendations from the Advisory Committee on Immunization Practices (ACIP) on best practices for use of the HPV vaccine. Currently, there are three HPV vaccines licensed for use in the United States: 1) pentavalent HPV vaccine (Gardisil-9, Merck and Co), 2) the quadrivalent vaccine (Gardasil, Merck and Co) and 3) the bivalent vaccine (Cervarix, GlaxoSmithKline). The first of these vaccines was the quadrivalent vaccine, which was licensed in 2006 for use in females aged 9-26 years old. That same year, the Advisory Committee on Immunization Practice (ACIP) recommended routine immunization with a 3-dose series of the quadrivalent HPV vaccine for females aged 11-12 years old, through age 26. It was not until 2009 that the ACIP permissively recommended the quadrivalent HPV vaccine for use in males (8). However, the ACIP did not expressly recommend routine HPV vaccination in males until 2011 (9). The bivalent vaccine was approved by the Food and Drug Administration (FDA) in 2009, and is only licensed for use in females as an alternative to the quadrivalent vaccine (10). In 2016, the ACIP issued an update for HPV vaccine recommendations stating that they recommend a 2-dose vaccine series, depending on the age that you receive vaccination (11). They state that older individuals, aged 15-26, and immune-compromised persons, should still follow the original 3-dose series schedule (11). While the vaccine is approved for a broad age range, the CDC and ACIP recommend that children receive their first dose when they are 11-12 years old. The recommendation is based on reasons, including: 1) vaccine is more immunogenic in younger versus older adolescents (12), 2) the vaccine is most effective when given prior to exposure to HPV, and exposure to HPV is associated with a persons' first sexual contact (13), and 3) other routine adolescent vaccines (TDaP, meningococcal

vaccine) are recommended to be given at ages 11-12, opening an ideal window for providers to administer this vaccine (14, 15).

Despite these recommendations, HPV vaccine uptake remains suboptimal. A report from 2015 showed that 60% of girls and 41.7% of boys received at least 1 dose of the vaccine, and only 39.7% of girls and 21.6% of boys completed the 3-dose series (16). Recommendations changed from a 3-dose to 2-dose series in 2016, although updated coverage reports have not been released since this change in recommendation. Attaining high vaccination rates among adolescents is essential to decreasing the burden of disease due to cervical cancer, and other cancers caused by HPV.

Understanding the factors that contribute to low vaccine uptake is crucial to successful HPV vaccination campaigns. Provider recommendation has been cited as an important factor for HPV vaccine uptake among parents (17-19); however, research has also shown that provider discomfort in discussing sexuality with parents is a significant barrier for providers when recommending HPV vaccination (20-22). Additionally, parents may deem the vaccine unnecessary as their child is not sexually active (17). However, this reasoning highlights the lack of parental appreciation of the HPV vaccine, as they miss the fundamental goal of vaccination as a prevention strategy provided prior to exposure (17, 23). These findings highlight a need for messaging to help parents and providers to identify the benefits of HPV vaccination and risks of persistent HPV infection as independent from the sexual nature of transmission of the virus.

Low uptake rates of the HPV vaccine have led to a series of campaigns to promote vaccination in young girls and boys. State and local health departments, NGOs in support of vaccination, and the CDC have carried out vaccine promotion efforts.

Information provided by the CDC in readily available online, and includes information about the vaccine and updated recommendations from the ACIP. These messages are meant to promote HPV vaccination, and focus on HPV as an infection, rather than potential cancer endpoints (6). For example, the HPV Vaccine Information Statement (VIS) has direct reference to HPV as a sexually transmitted disease, despite literature suggesting sexual reference is a factor contributing to vaccine refusal and delay (17, 21, 22). Additionally, these messages are not focused on perceived susceptibility of cervical cancer, or perceived severity of cervical cancer; even though these factors have been identified as predictive to vaccination status among adolescents (24). Furthermore, current messages that are promoted by the CDC are not disease salient on cervical cancer.

The study of fear appeals as a force of persuasion has been around for nearly 60 years (25). Evidence has shown mixed success with fear campaigns, leading to the development of the Extended Parallel Process Model (26). The Extended Parallel Process Model (EPPM) was conceptualized and developed to more fully understand the role of emotion in understanding how messages about health risks are processed (27). The EPPM postulates that fear based messages are comprised of four main components: self-efficacy, response-efficacy, susceptibility and severity. One's ultimate reaction to a fear-based message, according to the EPPM, is based on two reviews of that message. First, an individual will assess the threat presented in a message, conceptualized as perceived threat and comprised of susceptibility and severity. If an individual believes they are susceptible to a threat, and that the threat is a serious one, then they are motivated to begin the second appraisal of the message. The second appraisal evaluates the overall efficacy of the recommended response, which is conceptualized by perceived efficacy

and comprised of self-efficacy and response efficacy. The reaction to these two appraisals will determine if a persons' response to that message is adaptive or maladaptive (27).

The EPPM proposes various combinations of threat and efficacy that can influence the outcomes associated with exposure to health risk messages (28). First, the EPPM asserts that when individuals are exposed to health risk messages, they assess their risk and their susceptibility to the presented health threat. If an individual deems the health threat minor or insignificant, the message will not be processed further. Conversely, if the threat is perceived to be serious and relevant, an individual becomes scared. This fear prompts individuals to take action to reduce their fear. When people believe they are able to accomplish the recommended actions in response to the perceived threat (i.e., high perceived self-efficacy and response-efficacy), they are motivated to control the danger, and think about ways to move forward. When people to not believe they are able to accomplish the recommended actions in response to a perceived threat (i.e., low perceived self-efficacy) they are motivated to control their fear, rather than control dangers. Fear control leads to processes such as denial, defensive avoidance, and reactance (25). The EPPM provides a framework for understanding fear-based messaging, and how to harness danger centered processes and effect positive health change, as opposed to fear-centered processes, which often lead to denial and avoidance of important health issues.

Parental decision to vaccinate their children, specifically with the HPV vaccine, can be tied to multiple constructs of the Extended Parallel Process Model. These include perceived susceptibility of HPV infection (i.e., is my child at risk of infection), and

perceived severity of disease or health threat (29, 30). Research in this area has shown that these constructs are predictive of increased uptake of the HPV vaccine (31).

We do not believe that current messages from the CDC are focused on perceived susceptibility of cervical cancer, or perceived severity of cervical cancer - even though these factors have been identified in the literature as predictive to vaccination status among adolescents (24). Furthermore, these messages are not disease salient on cervical cancer, an additional potential limitation of the current messaging strategies. Based on these findings, we sought to create a new message framed with emphasis on disease threat and disease severity, and to promote self-efficacy for protection against cervical cancer through vaccination.

To the team's knowledge, this is the first time disease salient messaging approaches are assessed in a longitudinal, randomized trial setting in relation to uptake of the HPV vaccine. We hypothesize that a newly developed, cervical cancer targeted message will have an equal or stronger effect on intent to vaccinate with the HPV vaccine than the currently available message from the CDC, when compared to a non-vaccine control message. Our study findings can be used to inform future message testing strategies, and be scaled to test for effects in other populations of importance, such as adolescent males, or college-aged women.

Chapter II: Manuscript

Abstract

Introduction: Routine vaccination with the HPV vaccine is recommended for adolescents aged 11-12 years old, but uptake is suboptimal. Parents and providers are often uncomfortable discussing sexual practices of their adolescents, which have contributed to the delay or refusal of the HPV vaccine for the target age group. We created a cervical cancer salient message to promote HPV vaccination, by emphasizing disease salience and disease threat, while promoting self-efficacy. This trial tested the effects of a cervical cancer salient message on vaccine confidence and intent to vaccinate when compared to an infection salient message from the CDC and non-vaccine control.

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work should target groups with ‘Low’ or ‘Medium’ vaccine confidence at baseline as they may be more amenable to change, and more receptive to disease salient messaging.

Introduction

Human Papillomavirus (HPV) is the most common sexually transmitted infection in the United States (1). Persistent HPV infection can lead to cancer, with cervical cancer being the most common cancer caused by HPV(4). There is no cure for HPV, but HPV infections can be prevented through vaccination. Three HPV vaccines are currently licensed for use in the United States, and are given in 2 or 3 dose series depending on age at vaccination (11). The Centers for Disease Control (CDC) and Advisory Committee on Immunization Practices (ACIP) recommend that children receive the first dose when they are 11-12 years old. Factors contributing to the recommendation include: 1) the vaccine is more immunogenic in younger versus older adolescents (12), 2) the vaccine is most effective when given prior to exposure to HPV (13), and 3) other routine adolescent vaccines (Tdap, meningococcal vaccine) are recommended to be given at ages 11-12 (14, 15).

Despite being recommended for more than a decade, HPV vaccine uptake remains suboptimal (16). Provider recommendation has been cited as an important factor for HPV vaccine uptake among parents (17-19); however, research has also shown that provider discomfort when discussing child sexuality with parents is a significant barrier for providers in recommending HPV vaccination (20-22). Additionally, parents may deem the vaccine unnecessary as their child is not sexually active (17). However, this reasoning highlights the lack of parental appreciation of the HPV vaccine, as they miss the

fundamental goal of vaccination as a prevention strategy provided prior to exposure (17, 23).

Messages to promote HPV vaccination provided by the CDC focus on HPV as an infection, rather than potential cancer outcomes (6). For example, Vaccine Information Statement (VIS) has direct reference to HPV as a sexually transmitted disease, despite literature suggesting sexual reference is a factor contributing to vaccine refusal and delay (17, 21, 22). CDC messages are not focused on perceived susceptibility of cervical cancer, or perceived severity of cervical cancer; even though these factors have been identified as predictive to vaccination status among adolescents (24). Furthermore, current CDC messages are not disease salient on cervical cancer.

We sought to create a message to promote HPV vaccination, framed as a protection against cervical cancer with high emphasis on disease salience and disease threat, and designed to promote self-efficacy. This is the first time disease-salient messaging approaches have been applied to a randomized trial setting in relation to uptake of the HPV vaccine. We hypothesize that a cervical cancer targeted message will have an equal or stronger effect on intent to vaccinate than currently available messages from the CDC, compared to a control message.

Methods

This study was a 3-arm randomized trial, comparing three messages - a CDC HPV message, a cervical cancer salient message, and a non-vaccine control message - on attitudes towards vaccines and intent to vaccinate adolescents with the HPV vaccine. This study was conducted among parents of females 9-17 years old. Study participants were recruited online through Amazon Mechanical Turk, and followed for 2 weeks to assess

attitudes toward vaccination, vaccine confidence and intent to vaccinate before and after message delivery. Emory University approved all study activities. This trial is registered on ClinicalTrials.gov, under reference number NCT03002324.

Study Population

Men and women over the age of 18 who live in the United States, have at least one daughter between 9 and 17 years old, and have heard of HPV were eligible for our study. All recruitment, screening, and survey administration took place online through Amazon Mechanical Turk web services. Participants, regardless of eligibility, were given $0.05 for successfully completing the screening questions. Participants eligible to enroll in the study who finished the baseline survey were rewarded $0.95, to a total of $1.00. Participants who returned 2 weeks later to complete the follow-up survey were rewarded an additional $2.00, for a total $3.00 in compensation for all counted in the final sample.

Messages and Randomization Process

Participants randomized to the non-vaccine related control arm read a passage about bird feeding, which has been used as a control in similar trials (32, 33). Participants randomized to the CDC message arm read a message taken almost directly from the CDC VIS on HPV (6) that was minimally altered for length and clarity. Participants randomized to the cervical cancer messaging arm read a message developed by the study team. All were built to fall between 8.7-9.1, inclusively, on the Flesh-Kincaid grade level reading scale. This range was identified based on the reading level of the CDC message, and was used to keep reading level consistent and comparable to with what is currently in use.

Outcome Measures

There were two co-primary outcome measures in this study: 1) vaccine confidence, quantified by change in score on the Vaccine Confidence Scale (VCS), (34, 35) and 2) intent to vaccinate daughters with the HPV vaccine, measured through questions constructed by the study team. The VCS is an 8-point questionnaire built on identifying 'benefits', 'harms' and 'trust'. The response to each of these eight statements is a scaled response from 0 to 10, with higher score relating to positive attitudes towards vaccines (34). Overall VCS scores were calculated by averaging the numeric answers to the eight questions, while reverse coding the responses for the two 'harms' related questions. We assessed participant's scores on the VCS prior to message delivery, with comparison to scores after they received one of the randomized messages.

Intent to vaccinate against HPV was quantified in both surveys through a series of 3 questions. Participants were first asked if their daughter has received at least 1 dose of the HPV vaccine, to which they could answer 'Yes', 'No' or 'I don't know'. If participants answered 'Yes', they were asked about intent to have their daughter complete the vaccine series. If participants answered 'No' or 'I don't know', they were asked, "Do you intend to have your daughter start the HPV vaccine series?" Based on answers to these questions, participants' intent to vaccinate was dichotomized (intend to vaccinate/do not intend to vaccinate) for the analysis.

Survey Instrument

The baseline survey assessed participants' attitudes towards vaccines, quantified hesitance toward vaccines, knowledge of HPV, and sociodemographic characteristics.

Key sociodemographic data collected included the eligible child's age, parent age, race/ethnicity of parent, gender of parent, number of children in household, average income of household, marital status of participant and participants' education level. Questions used to assess participants' attitudes, knowledge, and beliefs during this study were adapted directly from the Vaccine Confidence Scale and the Parents' Attitudes about Childhood Vaccines (PACV) short scales (34-37). Participants were asked if their child has received at least one dose of HPV vaccine (yes/no/I don't know), and if they intend to complete the series (if yes) or their intent to vaccinate their child (if no or I don't know). The post intervention questionnaire included Vaccine Confidence Scale and PACV short scale questions, as well as 6 questions about overall engagement in the messages. Participants were again asked about their intent to either complete the vaccine series or intent to vaccinate their child with the HPV vaccine, dependent on their child's vaccine status.

Sample Size

Sample size calculations were completed using PASS (version 11, NCSS LLC, Kaysvile, Utah) using the one-way ANOVA procedure. A mean score of 8.19 (standard deviation= 3.0) on the Vaccine Confidence Scale was used as the baseline, based on the work of Gilkey et al on the Vaccine Confidence Scale (34). Calculations were done assuming an alpha of 0.05 and had 90% power detect a difference of 0.5 points in the Vaccine Confidence Scale in the CDC message arm, and a 1-point difference in the Vaccine Confidence Scale in the cervical cancer arm, compared to the bird-feeding control. Given these parameters, the proposed number of study participants was 699, with 233 participants in each study arm. We assumed 50% of participants would return for the second survey, and thus aimed to enroll 1,450 participants at baseline.

Statistical Analysis

Descriptive statistics were used to summarize participant sociodemographic characteristics. Bivariate analyses were conducted to assess randomization of sociodemographic characteristics by intervention arm using chi-square and t tests. Differences between post-intervention and baseline VCS scores were computed and used as a primary outcome. Mean differences in VCS scores were compared between each intervention arm and the control arm using unpaired t tests with unequal variance assumptions.

For all regression analyses, the sample was restricted to allow for comparisons between one intervention arm and the control arm, with independent comparisons between the CDC message and control arms, and the cervical cancer message and the control arms. Logistic regression models were used to compare respondents who reported an intent to vaccinate to those who did not report intent to vaccinate by intervention message. We stratified by baseline intention to vaccinate to account for prior intentions. Generalized linear regression models were run to examine the relationship between mean difference in VCS scores between each intervention arm and the control arm. Sociodemographic variables identified in bivariate analyses as significantly different between arms were included in the model as control variables.

Exploratory analyses were conducted to identify potentially sensitive subgroups of future interest, and also to understand overall engagement of participants with the intervention. Frequency statistics were calculated for a set of 6 engagement questions by intervention arm, which were all answered on a 7-point Likert-type scale of “Strongly Disagree” to “Strongly Agree” with the statement. Baseline and post intervention mean

VCS scores were grouped into three classes, “Low Confidence”, “Medium Confidence” and “High Confidence” according to standards established in prior literature, and differences in classification were examined by each intervention message (35). Additionally, VCS scores were calculated by the three factors identified in making the scale, ‘Benefits’, ‘Harms’, and ‘Trust’. Mean VCS scores by each factor were calculated at baseline and follow-up, and compared by message to identify if messages differentially affected populations by scale factor. When stratified by baseline confidence, change in intention to vaccinate was compared to assess if particular subgroups had a greater increase in intention to vaccinate by intervention message. All analyses were conducted in SAS 9.4 (Cary, NC) at an alpha level of 0.05.

Preliminary Results

A total of 14,165 participants were assessed for eligibility using Amazon Mechanical Turk. Of those, 1,223 participants were eligible for entry in the study, and 1,084 completed the baseline survey and were invited to participate in the second survey. Seven hundred and fifty participants were randomized to an intervention arm: 263 to the CDC message arm, 247 to the cervical cancer message arm, and 240 to the control message arm. The final study sample included 653 participants, with 60.2% of eligible sample accounted for in the analysis (Figure 1).

Most respondents were female (70.6%), white (75.0%) and married (77.2%) (Table 1). Total household income was evenly distributed between 6 categories, with 12.25% of the sample reporting earning less than $25,000 per year, and 20.37% of the sample reporting earning over $100,000 per year. The sample was evenly distributed by daughters’ age in three categories: 9-11 years old, 12-14 years old, and 15-17 years old.

A large proportion of the sample reported having some college education or college degree (68.5%). Bivariate analyses indicated a successful randomization, and identified baseline differences between daughters' age by intervention message received ($p < 0.05$) (Table 2).

We saw modest increases in VCS score when controlling for daughters age when comparing cervical cancer message arm and control arm, and CDC arm and control arm, however estimates were not statistically stable (Figure 2 and Table 3). When examining differences in VCS scores by the scale sub factors 'Benefits', 'Harms', and 'Trust', we saw the largest increase in benefits score in the CDC message arm (Table 4). When examining those who reported no intent to vaccinate at baseline, participants randomized to the cervical cancer message were 1.36 times more likely to report intent to vaccinate compared to control group (95% CI: 0.68, 2.71). Similarly, within the group reporting no intent to vaccinate at baseline, participants randomized to the CDC message were 1.25 times more likely to report intent to vaccinate compared to the control group (95% CI: 0.62, 2.33) (Table 5).

In secondary analysis, we found that 53% of the CDC message arm and 48% of the cervical cancer message arm agree or strongly agree with the statement, "I learned something from this passage about vaccines." When asked about the statement, "I could really relate to this passage." 52% of the CDC message arm and 51% of the cervical cancer message arm reported they agree or strongly agree with the statement. When looking at participants that reported low vaccine confidence at baseline, 14.5% changed intent to vaccinate from 'No' to 'Yes' in the cervical cancer arm, compared to 4.3% in the control and CDC message arm (Figure 3).

Discussion

Our study is the first to examine the effects of disease-salient messages on intent to vaccinate in a randomized setting. By incorporating current CDC messages into this study, we were able to provide an important and relevant comparison between our message and what is currently available. Our results suggest that neither message affected intention to vaccinate or overall vaccine confidence in the study population. Other studies have examined the effects of the HPV VIS on parental HPV vaccine acceptability. In a randomized study conducted by Dempsey et al, researchers found that parents given information about HPV were no more likely to be accepting of the HPV vaccine and no more likely to get their child vaccinated compared to parents given no information (38). Our study findings are in line with this work, and add that written information about HPV also does not increase parental intent to vaccinate their children, or overall confidence in vaccines.

The cervical cancer passage constructed by the study team was designed to induce participants to vaccinate against HPV. We focused on disease severity, disease threat, as and overall self-efficacy to get the vaccine because these constructs were identified in prior literature as predictive to vaccination (22, 24, 29-31). The Vaccine Confidence Scale, used in the study as a primary outcome, was developed to measure overall confidence in adolescent vaccines using three factors: benefits, harms and trust (34, 35). While the message developed by the study team does highlight the benefits of vaccination and the harms of cervical cancer it was not developed to align directly with the constructs of the Vaccine Confidence Scale. With this in mind, it is not entirely surprising that our message and the CDC message did not have drastic effects on overall

confidence by VCS standards. Additionally, our sample was heavily skewed at baseline to participants with ‘high’ confidence (45% of the sample), which was highly correlated with intent to vaccinate. The skewness of the sample is a possible explanation for the null result as well, because such a large portion of the sample intended to get their daughter vaccinated at baseline. Subgroup analyses suggest that within participants who had scores of ‘low’ confidence at baseline, there was more potential for change in intention by intervention message. Within this subgroup we saw the most movement in the cervical cancer intervention arm (Figure 3). These findings have potentially identified a sensitive subgroup, those initially having ‘low’ or ‘medium’ confidence at baseline, as targets for future studies. In light of these findings, it might be more appropriate for future studies to create a tailored intervention, using VCS as a means to identify the target population and assess vaccine intention as a primary endpoint.

Participants who saw the CDC and HPV message were equally engaged in their respective message compared to the bird-feeding control. Roughly 50% of the sample reported they learned something from the passage, and roughly 50% of the sample reported they could relate to the message (Figure 4 and Figure 5). We believe that employing different modes of delivery in future studies could increase overall engagement in our messages. Providing an audio-visual message, such as a short video clip, or purely visual message, such as an info graphic, could prove to be more successful than reading text paragraphs in getting our message across to parents and providers. Importantly, levels of engagement were consistent between our message and the CDC message, providing further evidence that what is currently available could be improved.

Strengths and Limitations

There were a number of strengths to this study, the largest being study design. Social desirability bias of our study participants was limited compared to other randomized messaging studies due to the online mode of data collection. Furthermore, given the online mode of collection we had a very high percent of our sample return for follow-up (60.2%), which limits bias in the sample due to loss-to-follow-up compared to other messaging studies. The generalizability of our sample to the United States population is comparable to other studies conducted through Amazon Mechanical Turk – and studies have found that populations accessed through Amazon Mechanical Turk are at least as representative to the U.S. population as traditional subject pools (39). With the strengths of the study come a few limitations. Mainly, the self-report nature of vaccine intentions and vaccine status provide a potential source of bias in our sample. However, given data were collected online, we have no reason to believe the participants intentionally provided misinformation (40).

Conclusion

Providing parents with a cervical cancer salient message or a HPV infection salient message had no effect on intention to vaccinate with the HPV vaccine or on overall vaccine confidence. While overall effects were null, subgroup analysis suggests that participants with a baseline ‘low’ or ‘medium’ confidence are more amendable to intervention, and more suitable as a target population for study. These conclusions highlight the need for additional research in this field to identify the best communication strategy to reach target immunization levels for the HPV vaccine.

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Tables

Table 1: Demographic Characteristics of study sample (n=658).

	n or mean	% or SD
Parent Gender		
Male	187	28.6
Female	461	70.6
Parent Age, Years	39.83	7.1
Parent Race/Ethnicity		
White	490	75.0
African American	41	6.3
Asian	37	5.7
Hispanic	29	4.4
American Indian, Alaska Native, Hawaiian, or Pacific Islander	34	5.2
Other or Multi-race	22	3.4
Parent Marital Status		
Single, Never Married	50	7.7
Married	504	77.2
Widowed/Divorced/Separated	99	15.2
Household Income		
Less than $25,000	80	12.3
$25,000 - $34,999	77	11.8
$35,000 - $49,999	97	14.9
$50,000 - $74,999	138	21.1
$75,000 - $99,999	128	19.6
Over $100,000	133	20.4
Number of children in household		
1 child	111	17.0
2 children	255	39.1
3 children	151	23.1
4 or more children	136	20.8
Parent Education Level		
High School or GED	65	9.7
College Degree	447	68.5
Graduate or Professional Degree	141	21.6
Daughter's Age		
9-11 years old	221	33.8
12-14 years old	207	31.7
15-17 years old	225	34.5

Table 2. Demographic Characteristics of study sample by randomized message.

	CDC Message (n=229)		Cervical Cancer Message (n=210)		Control Message (n=214)	
	n	**%**	**n**	**%**	**n**	**%**
Parent Gender						
Male	61	26.6	59	28.1	67	31.3
Female	167	72.9	149	71.0	145	67.8
Parent Age, Years	40.1	7.5	39	6.5	40	7.2
Parent Race/Ethnicity						
White	165	72.1	161	76.7	164	67.6
African American	18	7.9	15	7.1	8	3.7
Asian	16	7.0	7	3.3	14	6.5
Hispanic	12	5.2	8	3.8	9	4.2
American Indian, Alaska Native, Hawaiian, or Pacific Islander	12	5.2	10	4.8	12	5.6
Other or Multi-race	6	2.6	9	4.3	7	3.3
Parent Marital Status						
Single, Never Married	18	7.9	17	8.1	15	7.0
Married	179	78.2	155	73.8	170	79.4
Widowed/Divorced/Separated	32	14.0	38	18.1	29	13.6
Household Income						
Less than $25,000	33	14.4	23	11.0	24	11.2
$25,000 - $34,999	28	12.2	27	12.9	22	10.3
$35,000 - $49,999	26	11.4	32	15.2	39	18.2
$50,000 - $74,999	49	21.4	47	22.4	42	19.6
$75,000 - $99,999	42	18.3	43	20.5	43	20.1
Over $100,000	51	22.3	38	18.1	44	20.6
Number of children in household						
1 child	44	19.2	31	14.8	36	16.8
2 children	79	34.5	89	42.4	87	40.7
3 children	58	25.8	40	19.1	52	24.3
4 or more children	47	20.5	50	23.8	39	18.2
Parent Education Level						
High School or GED	27	11.8	16	7.6	22	10.3
College Degree	152	66.4	149	71.0	146	68.2
Graduate or Professional Degree	50	21.8	45	21.4	46	21.5
Daughter's Age						
9-11 years old	77	33.6	78	37.1	66	30.8
12-14 years old	86	37.6	48	22.9	73	34.1
15-17 years old	66	28.8	84	40.0	75	35.1

Table 3: Estimated Increase in Vaccine Confidence Scale Score by Intervention Message and 95% Confidence Intervals from Linear Risk Regression Models.

	Estimate	95% CI	
Cervical Cancer Message	0.152	-0.03	0.34
CDC Message	0.154	-0.03	0.34

Table 5: Estimated Risk Ratios and 95% Confidence Intervals for the Effect of Intervention Message on Intent to Vaccinate, Compared to Non-Vaccine Control

	Estimate	95% CI	
Intent to Vaccinate at Baseline			
Cervical Cancer Message	0.88	0.22	3.61
CDC Message	0.89	0.23	3.38
Do not Intent to Vaccinate at Baseline			
Cervical Cancer Message	1.36	0.68	2.71
CDC Message	1.26	0.62	2.58

Table 4: Mean Vaccine Confidence Scale (VCS) Scores for each message at baseline and follow-up, separated by scale factors.

	Scale Score (8 items)		Benefits (4 items)		Harms (2 items)		Trust (2 items)	
	Mean (SD)	**Difference (SD)**	**Mean (SD)**	**Difference (SD)**	**Mean (SD)**	**Difference (SD)**	**Mean (SD)**	**Difference (SD)**
Control Message								
Baseline	7.43 (1.99)	-0.06 (0.94)	7.82 (2.20)	-0.07 (1.08)	3.90 (2.73)	-0.2 (2.04)	7.98 (2.13)	-0.14 (1.51)
Post Message	7.35 (1.91)	n/a	7.74 (2.17)	n/a	3.88 (2.44)	n/a	7.85 (2.10)	n/a
CDC Message								
Baseline	7.45 (2.00)	0.09 (1.01)	7.75 (2.21)	0.18 (1.17)	3.61 (2.56)	0.4 (1.78)	7.89 (2.10)	0.06 (1.55)
Post Message	7.52 (1.91)	n/a	7.90 (2.17)	n/a	3.65 (2.51)	n/a	7.95 (2.05)	n/a
Cervical Cancer Message								
Baseline	7.18 (1.96)	0.08 (1.00)	7.49 (2.21)	0.10 (1.12)	3.81 (2.59)	-0.03 (2.03)	7.58 (2.09)	0.08 (1.37)
Post Message	7.29 (1.85)	n/a	7.60 (2.08)	n/a	3.78 (2.33)	n/a	7.67 (2.02)	n/a

Figures/Figure Legends

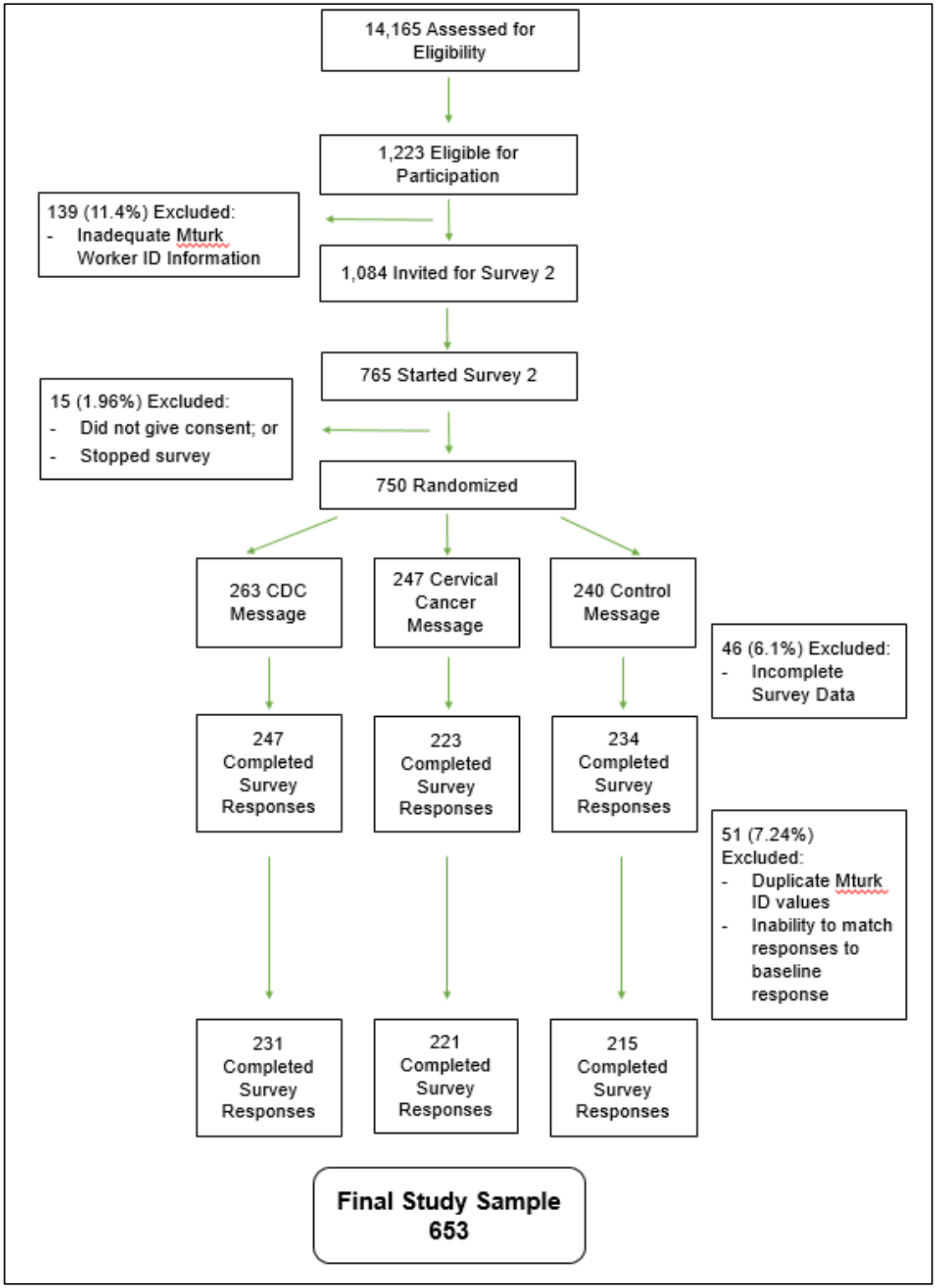

Figure 1: Study CONSORT Diagram: Selection, Inclusion and Exclusion Criteria, and Randomization.

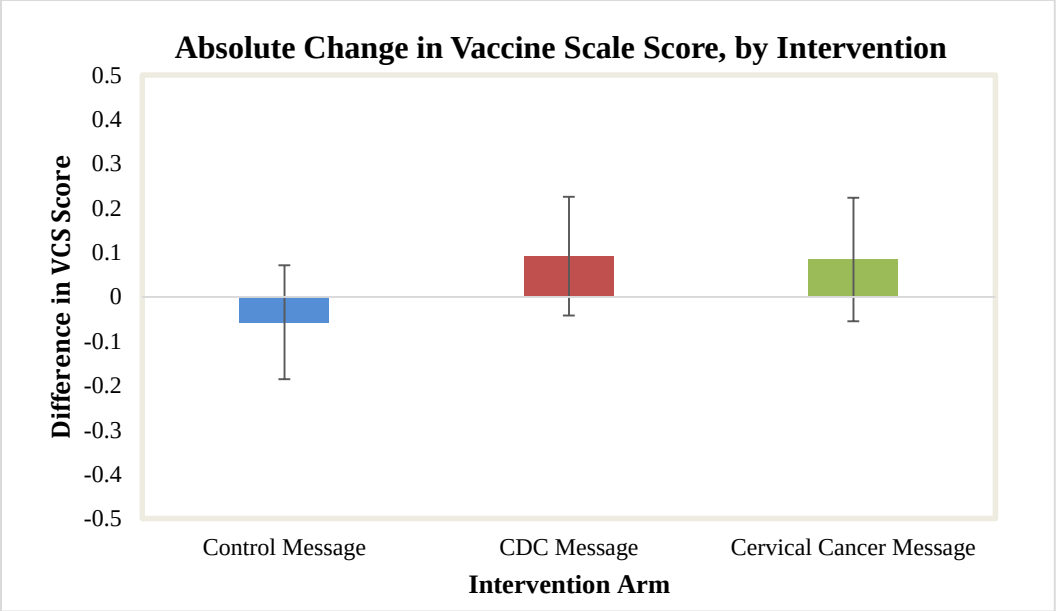

Figure 2: Point difference in Vaccine Confidence Scale Score by Intervention Arm, with corresponding 95% confidence intervals.

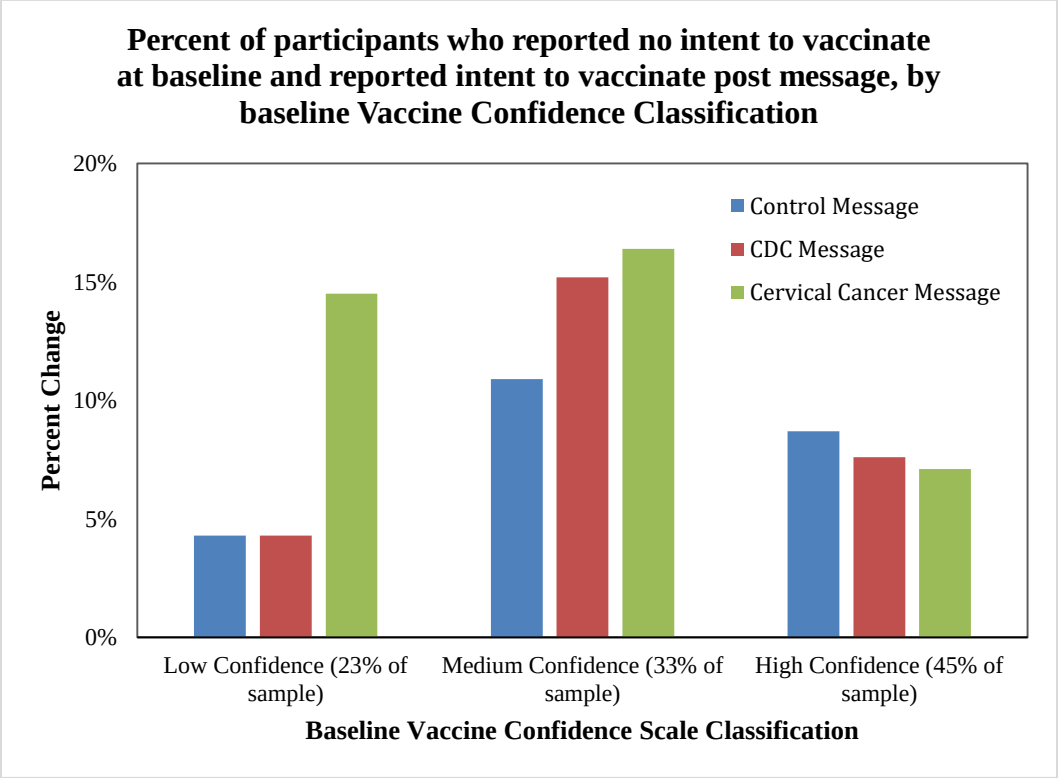

Figure 3: Participants who identified no intent to vaccinate at baseline, and shifted to reporting intent to vaccinate after reading the intervention message. 14.5% of participants with low vaccine confidence at baseline in the cervical cancer arm changed intentions, compared to 4.3% of participants with low vaccine confidence at baseline in the CDC and control arms.

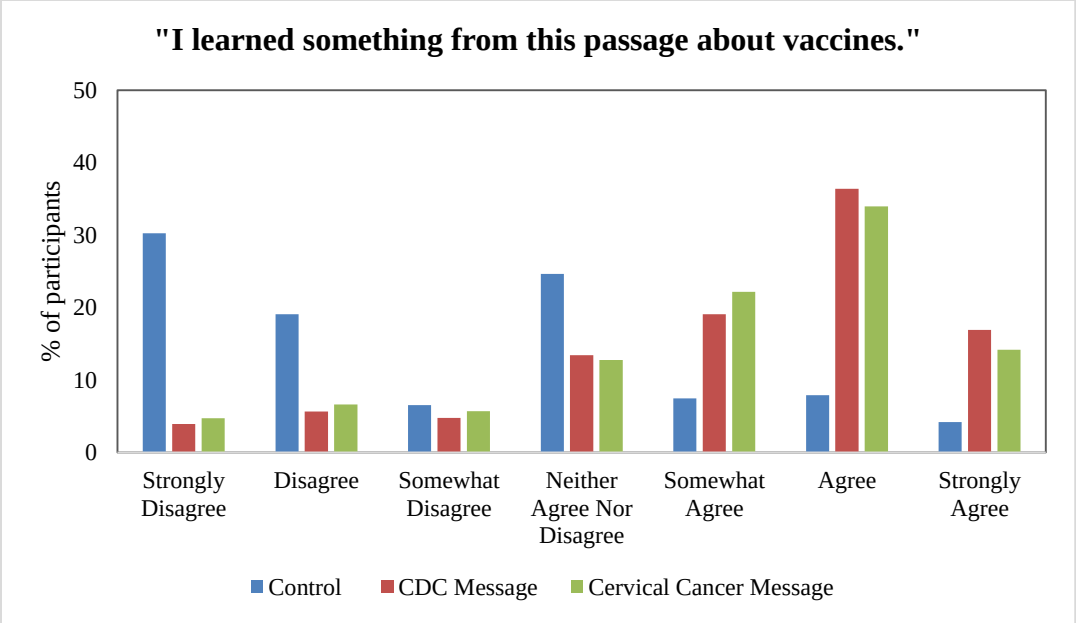

Figure 4: Participant responses to a 7-point Likert-Scale engagement question, “I learned something from this passage about vaccines.”, by intervention message.

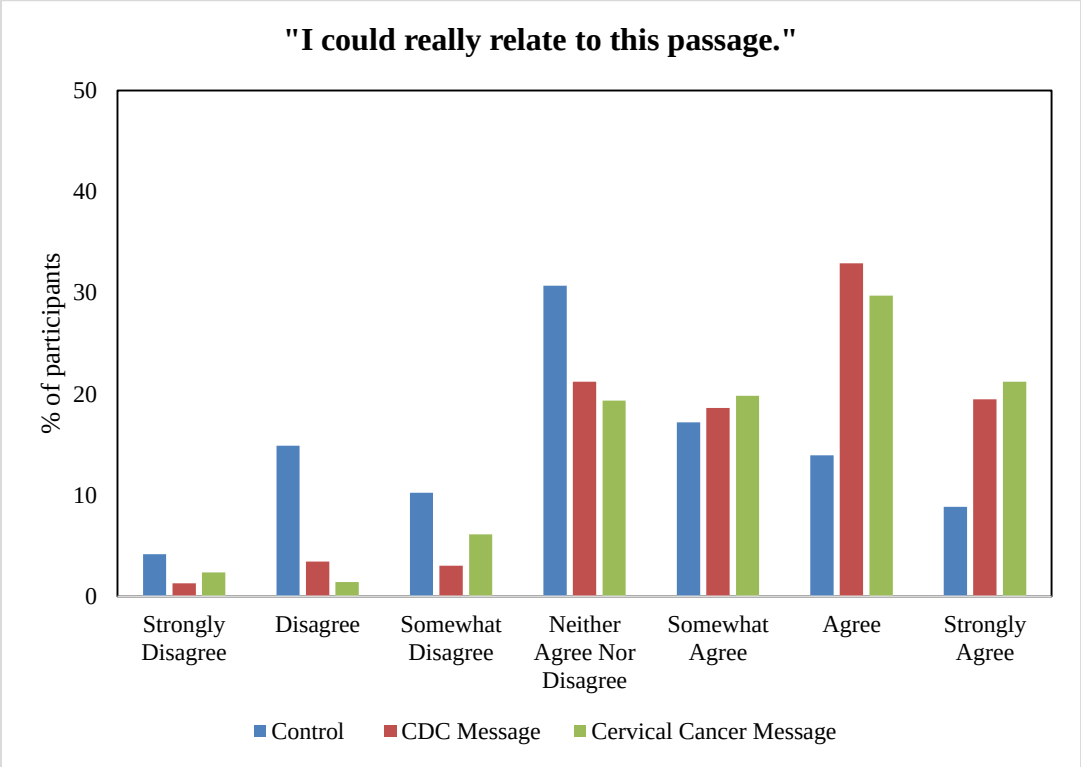

Figure 5: Participant responses to a 7-point Likert-Scale engagement question, “I could really relate to this passage.”, by intervention message.

Chapter III: Summary, Public Health Implications, Future Directions

The HPV vaccine is one of the first vaccine to provide protection against cancer outcomes, and as a result, the vaccine itself has major public health impacts in the long term. However, if uptake of the vaccine remains low, the potential long-term impacts of the vaccine may not be realized. For this reason, research in the field of public health communication is critical. Understanding how to most effectively communicate with vaccine hesitant parents and providers is paramount in decreasing the burden of disease due to vaccine preventable diseases and infections, such as HPV.

This work is the first to explore the impact of a cancer salient message strategy on intent to vaccinate with the HPV vaccine. While we did not find an overall effect on vaccine intention due to our message, we did potentially identify a sensitive subgroup for future interventions. Parents that identify at baseline as having low or medium confidence may be more amenable to a disease salient message rather than infection salient message. This is an important finding that warrants future research. Additionally, the results of this study shed light on the use of the Vaccine Confidence Scale in future studies. We used this scale as a way to measure change in confidence as an outcome, but have found the scale might be more useful in future interventions as a way to identify sensitive subgroups to target at baseline. Results from this study also affirmed results from prior studies in vaccine messaging that identified infection salient messaging strategies are not effective. These results provide more evidence in favor of studying messaging strategies, as what is currently in practice is not effective, and could explain some of why vaccine uptake with the HPV vaccine is below target levels.

As a part of this study, information was collected through during the baseline survey to identify behavioral biases. Future work with this dataset could use answers to the behavioral phenotyping questions to better understand if and how behavioral biases play into vaccine hesitancies. Results from an analysis of this nature could also provide novel insight into how to tailor messages to reach vaccine hesitant parents.

This study was also purposefully targeted to parents of adolescent girls, as the disease salient message was built around cervical cancer. Future studies in disease salient messaging could focus on a gender neutral disease outcome, such as oropharyngeal cancer, to see if this messaging strategy is equally or more effective in parents of adolescent males.