INDIVIDUAL-LEVEL AND CLINIC-LEVEL FACTORS ASSOCIATED WITH HPV VACCINE INITIATION AMONG 11-17 YEAR OLD ADOLESCENTS

by

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INDIVIDUAL-LEVEL AND CLINIC-LEVEL FACTORS ASSOCIATED WITH HPV VACCINE INITIATION AMONG 11-17 YEAR OLD ADOLESCENTS

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The human papillomavirus is the most common sexually transmitted infection, and persistent infection with oncogenic types can lead to cervical, anal, vaginal, vulvar, penile, and oropharyngeal cancers. HPV vaccination can protect against infection. However, vaccine series initiation and completion rates are below national goals. This dissertation aimed to identify individual- and clinic-level factors associated with HPV vaccination among adolescents aged 11-17 years to inform future interventions aimed at increasing vaccination and reducing HPV-related cancers.

This dissertation is in the form of three manuscripts each contributing to the overall aim. In manuscript 1, we conducted a systematic review of reviews identifying parental, provider, and clinic-level factors associated with HPV vaccination among adolescents. We synthesized findings from 12 reviews into a multilevel framework of HPV vaccination that can broaden our understanding of HPV vaccination and can inform future interventions by highlighting the relations between factors and potential intervention points. In manuscript 2, we examined correlates of parental intentions to vaccinate and parental psychosocial predictors of HPV vaccination for low income, underinsured Hispanic adolescent females.

Findings can inform the development of targeted interventions for this population. In manuscript 3, we identified clinic characteristics and Consolidated Framework for Implementation Science Inner Setting constructs associated with HPV vaccine series initiation rates within a pediatric clinic network. Understanding clinic-level factors associated with vaccination can inform implementation of clinic systems and policies aimed at increasing vaccination rates.

Overall, these manuscripts contribute to the literature examining multilevel factors associated with adolescent HPV vaccination. Findings inform future multilevel interventions aimed at increasing HPV vaccination and targeting parent-, provider-, and clinic-levels.

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BACKGROUND

The human papillomavirus (HPV) infects nearly 14 million Americans each year making it the most common sexually transmitted infection among sexually active individuals.[1] Specific types of the virus can cause genital warts, anogenital cancers, and oropharyngeal cancer. To protect against HPV-related cancers, the HPV vaccine is available for individuals ages 9-26 years, and the Centers for Disease Control and Prevention (CDC) recommends adolescent females and males receive the vaccine at ages 11-12 years. Despite this recommendation, HPV vaccine coverage in the United States falls below national targets.[2,3] To improve coverage, researchers need an understanding of the individual-level and clinic-level factors that influence vaccination in order to develop effective, multilevel interventions and to reach national vaccination targets. This dissertation aims to inform future multilevel intervention development by focusing on both individual- and clinic-level factors related to HPV vaccination. Specifically, this dissertation provides a conceptual framework of factors related to HPV vaccination among adolescents, describes predictors of HPV vaccination among female Hispanic adolescents, and examines clinic-level factors correlated with implementation of HPV vaccination guidelines.

Human papillomavirus

Currently, seventy-nine million Americans are infected with the human papillomavirus, and most sexually active individuals will contract HPV in their lifetime.[1] Over 40 types of the virus can infect the anogenital region, and most infections occur in individuals in their late teens or in their twenties.[1,4–6] While most infections clear on their own, persistent infection with specific types can lead to genital warts and to HPV-related cancers. Oncogenic types of HPV are linked to over 90% of cervical, anal, and rectal cancers, 75% of vaginal cancers, 70% of vulvar

and oropharyngeal cancers, and 63% of penile cancers.[7] Incidence of HPV-related cancers has increased over time with cervical and oropharyngeal cancers most commonly diagnosed in the United States.[7]

HPV vaccine

The HPV vaccine can protect against HPV types that cause genital warts and cancers, and the CDC Advisory Committee on Immunization Practices (ACIP) recommends the HPV vaccine as a part of the routine adolescent vaccination schedule.[8] In 2006, Gardasil-4 became the first HPV vaccine available and recommended to protect against low-risk types of the virus causing genital warts (HPV-6, -11) and high risk oncogenic types linked to HPV-related cancers (HPV-16, -18).[9,10] Cervarix, a bivalent vaccine available and recommended in 2010, also protects against oncogenic HPV-16 and -18.[11] Available since 2014, the nanovalent vaccine Gardasil-9 protects against nine HPV types causing genital warts and anogenital and oropharyngeal cancers (HPV-6, -11, -16, -18, -31, -33, -45, and -52).[12] Each HPV vaccine required a three-dose series for optimal protection until 2016 when the recommendations changed. New recommendations state that adolescents under 15 years required only two doses for optimal protection.[13] The vaccine is recommended for adolescents ages 11-12 years alongside other adolescent vaccinations. However, vaccination may start as young as nine, and the catch-up age range for both males and females is 13-26 years.[8]

Despite HPV vaccine recommendations by ACIP, vaccination remains below national benchmarks. Healthy People 2020 sets the goal that 80% of females and 80% of males complete the vaccination series by ages 13-15.[2] However, in 2014, series completion fell short with only 39.7% of females and 21.6% of males ages 13-17 years receiving all three doses.[3] Series

initiation was higher with 60% of females and 41.7% of males ages 13-17 years receiving at least one dose.[3]

Public Health Significance

Multiple factors at both the individual- and clinic-levels influence parents' decisions to vaccinate their children against HPV. These may include personal beliefs, perceived barriers, communication with physicians,[14–19] or clinic system factors.[18,20] Understanding how these factors influence parents' decisions is critical to designing effective multilevel interventions to increase HPV vaccination. Tailored multilevel interventions addressing populations with low vaccination rates and populations experiencing disproportionate HPV-related health outcomes can help reach national HPV vaccine benchmarks and alleviate later health disparities in HPV-related cancers.

Specific aims

This dissertation includes three aims that examine individual-level and clinic-level factors related to HPV vaccination among adolescents. The specific aims are:

1. To provide a multilevel framework of individual-, provider-, and clinic-level factors predicting and correlated with HPV vaccination among U.S. adolescents based on a systematic review of reviews;
2. To identify longitudinal psychosocial predictors influencing Hispanic mothers' decisions to vaccinate their adolescent daughters ages 11-17 years against HPV; and
3. To explore the relationship of four Consolidated Framework for Implementation Science Inner Setting constructs, culture, leadership engagement, learning climate, and available resources, with implementation of HPV vaccine guidelines.

Each aim is designed to inform future multilevel intervention development to increase HPV vaccination among adolescents aged 11-17 years. Aim 1 provides a multilevel framework of individual-, provider-, and clinic-level factors associated with HPV vaccination. The framework builds on previous work by Fernandez and colleagues who developed a multilevel framework to illustrate relationships between individual and environmental-level factors, HPV vaccine acceptance and willingness to vaccinate, and health outcomes.[18] The model included in this dissertation provides up-to-date factors associated with HPV vaccine uptake among both males and females. Such a multilevel framework can inform future intervention development by providing a succinct and clear picture of the multilevel factors influencing adolescent HPV uptake.

Aim 2 adds to the literature by specifying predictors of vaccination for Hispanic female adolescents, an important population to target due to cervical cancer morbidity and mortality disparities.[7,21] Aim 2 utilizes data from *Por Nuestras Hijas* (PNH), a group randomized controlled trial, to identify psychosocial predictors of vaccination. The trial assesses the effectiveness of two educational interventions aimed at increasing HPV vaccination among Hispanic adolescent females. Intervention developers used the Fernandez et al. multilevel framework to guide intervention methods, strategies, and messages.[18,22]

Aim 3 relates to clinic-level factors that are associated with implementation of HPV vaccination guidelines. Currently, PNH is expanding to include a provider and clinic-level intervention component. Providers and clinic-level factors are critical to increasing HPV vaccination,[14–19] and there is a need to understand the contextual factors associated with implementing HPV vaccination guidelines to inform development of multilevel interventions

such as PNH.[23] Understanding clinic factors associated with variable HPV vaccination rates across clinics can help intervention developers identify potentially modifiable factors on which to intervene.

JOURNAL ARTICLE 1

Individual, Provider, and Clinic-Level Factors Associated with HPV Vaccine Uptake by Females and Males 11-17 Years: A Systematic Review of Reviews

Target Journal: American Journal of Public Health

Abstract

Background. Multilevel models of HPV vaccination among adolescents are needed to inform interventions aimed at increasing HPV vaccination. While models exist depicting factors associated with HVP vaccination among females, there are no models incorporating factors for males. Further, no models examine factors associated with both initiation and completion. Therefore, this systematic review of reviews aimed to provide a multilevel framework of individual-, provider-, and clinic-level factors predicting and correlated with HPV vaccination among U.S. adolescents.

Methods. We searched Medline, Pubmed, PsychInfo, CINAHL, and ERIC databases for reviews conducted between 2006 and February 1, 2017 that identified correlates or predictors of HPV vaccination among adolescent males and females in the U.S. We identified parental-, provider-, and clinic-level factors associated with vaccination in each to inform a multilevel framework of adolescent HPV vaccination.

Results. We identified 12 eligible reviews. Parental factors associated with HPV vaccination included: knowledge; intentions; beliefs about perceived benefits of the vaccine, perceived risk of the adolescent contracting HPV or an HPV-related disease, perceived vaccine effectiveness, perceived safety, and perceived need for the vaccine; and attitudes. Parental behaviors associated with vaccination included interaction with the healthcare system and

communication with their adolescent. Provider factors associated with vaccination included provider recommendations and communication with parents, knowledge, and beliefs. Clinic-level factors associated with vaccination included provider audit and feedback systems and patient reminder systems.

Conclusion. A comprehensive multilevel framework that incorporates parent-, provider, and clinic-level factors associated with HPV vaccination highlights potential intervention targets. Intervention developers may use this model to identify specific factors to intervene on at these three levels in order to increase HPV vaccination among both male and female adolescents.

Background

The human papillomavirus (HPV) is the most common sexually transmitted infection in the United States. An estimated 80% of sexually active individuals will contract HPV in their lifetime.[6] Persistent infection with oncogenic types can lead to genital warts and cancer. HPV-related cancers include cervical, anal, rectal, vaginal, vulvar, penile, and oropharyngeal cancers with the most common being cervical cancer among women and oropharyngeal cancers among men.[7] The HPV vaccine became available for females in 2006 and for males in 2010, and the vaccine can protect against HPV-related cancers and genital warts. However, vaccination coverage remains lower than national goals.[3] The CDC Advisory Committee for Immunization Practices (ACIP) recommends the vaccine be administered to 11-12 year olds although it is available for adolescents starting at age nine and young adults up to age 26. Healthy People 2020 sets the goal that 80% of 13-15 year olds complete the multi-dose series.[2] In 2014, 60% of females ages 13-17 and 41.7% of males ages 13-17 initiated the HPV vaccine series. Series completion rates were lower with only 39.7% of females ages 13-17 and 21.6% of males ages

13-17 receiving all three doses.[3] Updated recommendations moving from a three-dose vaccine series to a two-dose series for some adolescents may help increase completion rates. However, evidence is lacking thus far due to due the novelty of the recommendations.

To increase HPV vaccination coverage among adolescents, it is important to understand the diverse factors associated with HPV vaccination at multiple levels. This includes understanding factors that influence parental decision-making about HPV vaccination and provider- and clinic-level factors associated with vaccination. Synthesizing and illustrating these factors in a multilevel framework can inform future interventions aiming to increase vaccination.

Multilevel models and evidence syntheses of factors associated with vaccination among adolescent females exist.[24,16,18,25] Early models focused exclusively on vaccine acceptance among females as proxy indicators of uptake[18] while more recent models have included vaccination initiation as the outcome of interest.[24,16,25] No models include male adolescents which may be due to the vaccine being available later for males than females.[26] Further, health behavior theories and sociocultural theories have been used to describe HPV vaccination behaviors.[27–29] Frameworks with theoretical underpinnings are needed. However, many do not move beyond individual or interpersonal factors influencing vaccination decision-making. This limits their ability to inform interventions that can impact broader clinic-level factors associated with vaccination.[30] The National Cancer Institute (NCI) specifically calls for multilevel interventions across the cancer control continuum.[31] A multilevel model of HPV vaccination that integrates individual-, interpersonal-, and clinic-level factors correlated with and predicting HPV vaccination can inform multilevel intervention development and meet NCI's call to action.

Fernandez and colleagues developed a multilevel framework of HPV vaccine acceptance and described parental, provider and system level factors influencing HPV vaccination acceptance. The frameworks was designed to inform intervention development at multiple levels including the individual-, interpersonal-, and clinic-levels.[18] The framework was among the first to illustrate the multilevel influences on HPV vaccine acceptance and willingness including studies that focuses on both parents and young adults. Limitations of the Fernandez framework, however, was that the majority of studies available failed to include vaccination behavior as the outcome. A new framework to describe multilevel influences of actual HPV vaccination is needed..

Therefore, this systematic review of reviews aims to provide a multilevel framework of individual-, provider-, and clinic-level factors predicting and correlated with HPV vaccination among U.S. adolescents. As Fernandez and colleagues did, this model follows a framework structure for organizing needs assessment information first described by Green and Kreuter[32] and further developed by Bartholomew Eldredge and colleagues[22] that is used for multilevel intervention development. This systematic review relies on reviews, defined as systematic, integrated, and literature reviews, as opposed to primary studies in order to consolidate the large body literature focused on correlates and predictors of HPV vaccination among adolescents in the U.S.

Methods

Methods are reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist.[33] To ensure quality, this review follows AMSTAR, a tool to assess the quality of execution of systematic reviews[34] modified to incorporate methods

for conducting systematic reviews of reviews.[35] This review is registered with PROSPERO (registration number: CRD42016044092). Authors SAR and DML screened, reviewed, and extracted data from reviews. Authors MEF and PDM served as content and methods consultants throughout the screening, review, data extraction process, analysis, and reporting process.

Eligibility criteria

The publication dates of included reviews were restricted to 2006 when the U.S. Food and Drug Administration approved the first available HPV vaccine[10] through the date of the final search (February 1, 2017). Reviews were defined as systematic reviews, integrated reviews, and literature views. Reviews reporting correlates and predictors of HPV vaccine initiation and/or completion for adolescents ages 9-17 years were eligible. Reviews must have reported outcomes that included 1) initiation of the 3-dose HPV vaccine series, and/or 2) receipt of subsequent doses, including completion of the 3-dose series measured by medical records review or parent report. Reviews that included only HPV vaccine awareness, acceptability, and intention outcomes were excluded. Only English language systematic reviews published in peer-reviewed journals were included. Comments, editorials, dissertations, abstracts, and conference proceedings were excluded. Reviews including only qualitative primary studies were excluded. However, reviews were included if a they contained findings based on mixed methods research or it qualitative data was presented with quantitative data corroborating findings.

Information sources and search strategies

We searched Medline (Ovid), Pubmed (NLM), PsychInfo (Ovid), CINAHL (Ebsco), and ERIC (Ebsco). A health sciences librarian experienced in developing and documenting search strategies for systematic reviews assisted in developing the search strategy. Concepts in the

search included human papillomavirus, immunizations or vaccination, parents or guardians, and adolescents. A combination of MeSH terms and title, abstract, and keywords were used to develop the initial Medline search and then adapted for other databases (see Supplemental Materials). After conducting the search and screening process, DLM examined article reference lists to identify cited reviews or studies not captured in the search.

Study Selection

Data management. All search results were downloaded to RefWorks v.2.0 (ProQuest), an online bibliographic management program, and duplicate bibliographies were removed. Reviewers used data collection and data management systems specifically designed for systematic reviews.[36] These included Excel workbooks for title and abstract screening, full text reviews, calculating interrater reliability, and producing PRISMA flowcharts.[37] Reviewers developed, pilot tested, and refined screening criteria questions for title and abstract screening and for full text reviews.

Screening process. SAR and DML independently screened all titles and abstracts against the eligibility criteria, and chose "No" or "Maybe" for each in the Excel workbook. A random sample of 65 systematic review titles and abstracts were selected to assess interrater reliability and calculate Cohen's Kappa (κ=0.85). Disagreements were resolved through discussions between the screeners. The reviewers were blind to the journal titles, authors, and author affiliations during title and abstract screening. Reviewers conducted full text reviews of the "maybes" from the title and abstract screening to determine final eligibility. Reviewers discussed disagreements and consulted with additional authors (MEF and PDM) as needed.

Data collection

SAR and DML independently extracted data for all eligible reviews. Data extracted included: review aims and/or study questions; search time period; number of publications and studies included; inclusion and exclusion criteria; population and setting; and factors associated with HPV vaccine series initiation and completion. Individual-, provider-, and clinic-level factors were categorized as either positively or negatively associated with HPV vaccine initiation or completion. Reviewers extracted factors that met one of two criteria: 1) authors presented statistical data illustrating the association between a factor and HPV vaccine outcomes in the text or a table; and/or 2) authors presented a general statement of findings in table format including the direction of the association between the factor and HPV vaccination outcomes.

We originally separated factors by those associated with uptake among males versus females. However, reviews that included both males and females did not typically identify factors related to vaccination by sex making it difficult to attribute factors to one sex or another. Additionally, in examining factors that were classified by sex among we observed little to no difference between them (i.e. the same factors were identified for both males and females). Therefore, we determined there was no need to create separate frameworks for males and females. Similarly, we originally extracted and separated factors based on those associated with HPV vaccine series initiation versus completion. In our analysis, we interpreted "uptake" as initiation only. As with sex, factors associated with initiation versus completion were not significantly different and did not require a second framework.

After independently extracting data, SAR and DML discussed each review to ensure all data were extracted. SAR catalogued all primary studies cited in each review to determine the amount of overlap between reviews.

Quality assessment

We used AMSTAR,[34] an eleven item checklist to assess the methodological quality of reviews included in this study. SAR and DLM independently applied the checklist. For each item in the checklist, SAR and DLM marked yes, no, can't answer, or not applicable for the AMSTAR criteria. SAR and DLM discussed discrepancies to finalize AMSTAR scores for each review. All yeses were summed to give each review an overall AMSTAR score. Total scores were categorized according to AMSTAR as low (range 0-3), mid-range (range 4-7), or high (9-11).

Multilevel framework development

Data were synthesized to produce a multilevel framework of HPV vaccination. Authors examined all factors associated with HPV vaccination and categorized factors as being at the individual-, provider, and clinic-levels. Factors were divided into six categories: 1) adolescent and parent socio-demographic factors, 2) parent psychosocial factors, 3) parent behaviors, 4) provider psychosocial factors, 5) provider behaviors, and 6) clinic systems or policies. Socio-demographic factors were not included in the multilevel framework of HPV vaccination as modifiable targets for interventions. The authors synthesized parental psychosocial variables by grouping all factors with the same theoretical construct names. When a review did not label factors as theoretical constructs, we labeled the factors based on our knowledge of health promotion theories and discussed the most appropriate fit. We compared author-provided

definitions when available to standard definitions in the National Cancer Institute Grid Enabled Measures Database (NCI GEM) to identify constructs. All constructs were combined into one multilevel framework illustrating the relations and potential causal pathways among individual-, provider-, and clinic-level factors associated with HPV vaccination.

Results

Study Selection

We identified 161 unique reviews from the database search and 10 additional reviews from reference list searches (Figure 1). Twelve reviews met criteria after the two-step screening process. [38–41,15,42–44,20,14,45,46] Principal reasons for exclusion after full text review were as follows: not a review (k=8), reviews of qualitative studies only (k=1), outcomes did not assess HPV vaccine initiation or completion (k=9), and review did not separate HPV vaccination outcomes from other vaccines (k=1). See Supplemental Materials for citations of excluded publications.

Characteristics of reviews

Reviews varied in populations, settings, types of primary studies included, and factors assessed (Table 1). More reviews examined factors associated with vaccination among female adolescents only (k=6)[38–40,42,20,45] than those that examined vaccination among male adolescents only (k=1).[44] The remaining five reviews examined vaccination among both females and males.[41,15,43,14,46] The earliest review concluded in December 2010[38] while the most recent review concluded July 10, 2015.[44] Five reviews included HPV vaccine series completion as an outcome while others were focused on initiation or uptake.[39–43]

Only one review included a meta-analysis.[39] The remainder used qualitative methods to reach their conclusions. The number of primary studies included in reviews ranged from 14 studies[38,43] to 67 studies.[40] We retrieved 264 unique primary studies with 77 studies included in more than one reviews. We were unable to retrieve complete bibliographies for two reviews.[41,45] One primary study appeared in five reviews.[47] We concluded that the overlap of primary studies in reviews was not significant, and we did not believe the factors associated with vaccination were overstated due to the overlapping primary studies. Reviews often cited multiple primary studies to describe factors associated with HPV vaccination. See Supplemental Materials for all unique primary studies and reviews citing each. Finally, only five of the twelve reviews reported searching gray literature.

AMSTAR scores ranged from 0[15,45] to 8.[41] Strict AMSTAR guidelines for "yes" responses to checklist items prohibited us from selecting "yes" when a review partially met a criterion, as many did. For example, some reviews noted two reviewers conducted data extraction but were ambiguous on whether there were two reviewers for screening.[43,44,14,46] AMSTAR requires explicit statements for both, and we selected "no" or "can't answer". AMSTAR scores were based solely on author reporting and may not reflect the methods actually used for a review if authors' statements were less explicit than required to confirm AMSTAR elements. All reviews were included in data synthesis for the multilevel framework despite AMSTAR scores. Because themes were consistent between low-scored and high-scored reviews (Table 2), we did not deem it necessary to use data from mid-range or highly scored reviews only.

Demographic factors associated with HPV vaccination

Nine reviews, including the meta-analysis described parent and adolescent demographics associated with HPV series initiation and completion.[38,40,41,15,42,20,14,45,48] These factors represent potential target populations and audiences for interventions aiming to increase HPV vaccination.

Adolescent race/ethnicity. Six reviews described HPV vaccine series initiation and completion by race/ethnicity.[39–41,15,42,45] In two reviews, being Hispanic or non-Hispanic White was positively associated with series initiation among adolescent females, and being non-Hispanic White was positively associated with series completion.[40,42] The meta-analysis found that being Black was negatively associated with HPV vaccine series initiation for females.[39] Two reviews identified Hispanic and Black race/ethnicities were negatively associated with series completion.[41,15] Using the more general category of "underserved and disadvantaged populations", culture and immigration status was negatively associated with initiation.[15] At the provider-level, one review that investigated provider-level behavior associated with patient race/ethnicity concluded that providers were less likely to educate parents of minority race/ethnicity adolescents and less likely to recommend the vaccine to them.[45]

Adolescent age. Three reviews described mixed findings relating adolescent age and HPV vaccination.[40,41,15] Two reviews described young age to be positively associated with series completion[41,15] while one review identified older age to be positively associated with series completion.[40] At the provider level, one review found that providers were more likely to vaccinate older versus younger adolescents.[15]

Adolescent sex. One review described being female versus male as positively associated with HPV vaccine series completion.[41] Another described provider preferences for vaccinating females over males.[15]

Adolescent insurance status. Five reviews including the meta-analysis described mixed results about the relation between adolescent insurance status and vaccine initiation and completion.[39,15,42,45,49] One review described a positive association between having insurance and series initiation for females[49] and another found a positive association with series completion.[42] However, the meta-analysis[22] and another review[31] found adolescents with insurance to be less likely to initiate the series compared to those without health insurance. Two reviews found the opposite. Lack of health insurance was negatively associated with series initiation for females and among underserved or disadvantaged populations and with series completion.[15,42] At the provider level, one review described providers concerns about reimbursement or adolescent insurance coverage to be negatively associated with series intiaition.[15]

Household income. Two reviews described the relation between household income and series initiation.[39,40] The meta-analysis found no association between low income and HPV vaccine series initiation, [39] although a review that broke down household income more finely found that very low income (133% to <322% of the federal poverty level) was positively associated with series completion by females.[40]

Three reviews described the relation between vaccine cost and vaccination.[38,15,45] Parental concerns about the cost of the vaccine were negatively associated with HPV vaccine series initiation by both females[38,45] and males.[15]

Parent education. One review described higher maternal education level as positively associated with completion rates.[41] However, the meta-analysis found no association between initiation and caregiver educational attainment.[39]

Parental psychosocial factors associated with HPV vaccination

Eight reviews described psychosocial factors associated with HPV vaccination.[38,40,15,42,44,20,14,45] We identified four overarching categories of psychosocial factors including: knowledge, intentions, beliefs, and attitudes. Beliefs were grouped into five subcategories: perceived benefits of the vaccine, perceived risk of the adolescent to contracting HPV or an HPV-related disease, perceived effectiveness of the vaccine, perceived safety, and perceived need for the vaccine. We integrated all psychosocial factors into the individual-level component of the multilevel framework.

Knowledge. Six reviews described the relation between knowledge and HPV vaccination, including sources of information about the vaccine.[38,40,15,42,20,45] Only one review included information about males.[15]

There were mixed results on the association of knowledge of HPV and the HPV vaccine and initiation. One review identified higher parental knowledge about the HPV vaccine as positively associated with HPV vaccine initiation by females.[42] Other reviews found mixed results [20] or no association.[40] Two reviews identified lack of knowledge as a barrier for vaccination among both adolescent males and females.[15,45] Specifically, limited parental knowledge about HPV and the HPV vaccine was negatively associated with vaccination among underserved and disadvantaged populations, and parents expressed a need for more information about the vaccine.[15] Knowledge-related barriers to vaccination included lack of knowledge that

the vaccine is available for males,[15] how to pay for the vaccine,[45] where to go for the vaccine,[15] and knowing the vaccine is a multi-dose series, which could hinder series completion.[15]

Reviews also highlighted parents' desires for accurate information to increase knowledge.[38] Parents perceive the source of the information they receive about HPV as important, and trusted information sources included family, friends, brochures, newspapers, and healthcare providers.[42,20]

Intentions. One review identified parental intention to vaccinate as a factor related to HPV vaccine series initiation among males.[44] No other reviews discussed parental intentions.

Beliefs. Eight reviews described parental beliefs related to the HPV vaccine initiation, including perceived benefits of the vaccine,[15,44,45] perceived vaccine effectiveness,[40,45] perceived vaccine safety,[38,40,15,42,14,45,49] perceived risk of adolescent's contracting HPV or developing an HPV-related disease,[15,14,45,49] and perceived need for the vaccine.[38,15,14,45] Five reviews focused exclusively on females[38,40,42,20,45] while two reviews included male and female adolescent populations.[15,14]

Positive perceived benefits of the vaccine, including protecting daughters from harm[45] and protecting sons' future partners from HPV,[44] were associated with series initiation. In one review identifying barriers to HPV vaccination, lack of parental perceived benefits was negatively associated with initiation among males.[15] Two reviews linked vaccine initiation among females with parents' positive perceptions about vaccine effectiveness in protecting against HPV and HPV-related cancers.[40,45] Parental perception that the HPV vaccine was safe for daughters was positively associated with series initiation among African American and Latina females.[40] Two reviews described general parental concerns about the HPV vaccine's safety to

be negatively associated with HPV vaccine initiation among female adolescents.[20,45] One review described similar findings for both male and female adolescents.[15] Other reviews specified parental safety concerns including concerns about side effects,[38,15,42] concerns about the safety of too many vaccines,[14] and concerns about the vaccine being too new.[15]

Parents' beliefs that their sons or daughters were at risk of future HPV infection or HPV-related diseases were also related to initiation.[15,20,14] A review concluded that lack of perceived risk was associated with lower likelihood of initiation.[45] Parental perceptions of whether their adolescent needed the HPV vaccine were also associated with vaccine initiation.[38,15,14,45] One review described lack of parental perceived need for the vaccine as a barrier to series initiation for male adolescents.[15] A second review described similar findings for adolescent females.[38] Reviews described parental beliefs that their adolescent was "too young" as a reason he or she did not "need" the vaccine.[38,15,14,45] One review noted that initiation was more likely if parents thought their adolescent was sexually active, i.e., the vaccine was "needed" to protect against infection.[14] Other reviews found when parents believed the vaccine would encourage sexual activity or they did not perceive their adolescent as sexually active, then they did not endorse the idea that the vaccine was needed; and those beliefs were barriers to initiation.[38,14]

Attitudes. One review found mothers' attitudes towards their own cervical cancer prevention behaviors linked to HPV vaccine initiation for adolescent females.[38] A second review identified parental distrust of the healthcare system as a barrier to vaccine initiation among underserved and disadvantaged adolescents.[15]

Parent behaviors associated with HPV vaccination

Seven reviews described parent behaviors associated with HPV vaccination.[38,41,15,42,44,20,14] We integrated these behaviors into the multilevel framework of HPV vaccination as potentially modifiable behaviors for interventions to target.

Interaction with the healthcare system. Seven reviews described the relation between HPV vaccination and parent or adolescent interactions with the healthcare system.[38,41,15,42,44,20,14] One review found that parental preventative care behaviors were associated with adolescent HPV vaccine completion.[41] Higher parental preventative healthcare behaviors, and therefore higher levels of interaction with the healthcare system, were linked to vaccine completion. Preventative healthcare for adolescents was also linked to HPV vaccination. Previous receipt of the meningitis or MMR vaccines was associated with series initiation[42] while previous parental refusal for vaccination was a barrier to initiation.[14]

Adolescent contact with the healthcare system, such as regular visits with a provider, was also linked to vaccination outcomes.[38,15] Three reviews noted that recent visits to the doctor and visits with a healthcare provider in the previous twelve months were linked to HPV vaccine initiation for both male and female adolescents.[42,44,20] Lack of a medical home was negatively associated with series completion in one review.[15]

Two reviews described the relation between healthcare settings and HPV vaccination.[38,15] Care in an outpatient setting was linked to vaccine initiation for female adolescents, while care in hospitals or emergency departments was a barrier to initiation.[38] Finally, care with a pediatrician or gynecologist was associated with series completion for females in one review.[15]

Communication. One review described the association between parental-child communication and HPV vaccination.[44] Increased communication about the HPV vaccine between parents and their adolescent sons was associated with HPV vaccine initiation.

Provider-level factors associated with HPV vaccination

Seven reviews described provider-level factors associated with HPV vaccine series initiation and completion.[38,40,15,42,20,14,45] We included these factor in the multilevel framework of HPV vaccination as modifiable targets for provider-level interventions.

Provider recommendation and communication with parents. Reviews consistently highlighted the association between providers recommendation of the HPV vaccine and vaccination outcomes. Five reviews described the positive association between provider recommendations and HPV vaccine series initiation among adolescent females.[38,40,42,20,45] Two reviews described the same association for males.[15,14] The two reviews also described the lack of provider recommendation as negatively associated with HPV vaccination.[15,45] The way providers present the HPV vaccine is also important. One review described providers recommendation styles, such as risk-based approaches or treating the vaccine as different from other adolescent vaccines, as negatively associated with series initiation.[15]

Psychosocial factors. Two reviews described provider psychosocial factors associated with HPV vaccine series initiation.[15,45] One review described gaps in provider knowledge as negatively related to HPV vaccine series initiation.[15] Specifically, some providers may not recommend the vaccine due to low knowledge about the link between HPV and HPV-related diseases other than cervical cancer.

The reviews also described provider beliefs negatively associated with HPV vaccination. These included provider beliefs about parental concerns,[15] beliefs about parental attitudes towards the vaccine,[15] and the lack of perceived need for the adolescent patient to receive the vaccine.[45]

Finally, one review identified provider discomfort discussing the HPV vaccine as a barrier to series initiation.[45] Providers' apprehension to discuss the risks or benefits of the vaccine was negatively associated with initiation. Similarly, apprehension to discuss sexuality or sexually transmitted infections with parents or adolescents was negatively associated with initiation.

Clinic-level factors associated with HPV vaccination

We identified two predominant clinic-level systems associated with HPV vaccine series initiation and completion: provider-targeted systems[46] and patient-targeted reminds.[43,46] These systems were integrated into the clinic-level component in the multilevel framework of HPV vaccination.

Provider-targeted systems. Provider-targeted systems associated with vaccination in adolescents included provider audit and feedback systems, provider alerts, and provider scripts.[46] One specific program described was the CDC's quality improvement program Assessment, Feedback, Incentives, and eXchange (AFIX)[50] which was linked to increases in HPV vaccine series initiation and completion in clinics implementing the program.[46]

Patient-targeted reminder systems. Both reviews described patient-targeted reminder systems associated with HPV initiation and completion among adolescents. These included patient reminder/recall systems such as text messages, letters, telephone calls or outreach

visits.[43,46] Both provider-targeted systems and patient-targeted interventions have been associated with HPV vaccine initiation and completion. However, evidence suggests provider-targeted interventions are more successful to increase series initiation, and parent-targeted reminders are more successful to increase series completion.[46]

Discussion

We synthesized individual-, provider, and clinic-level factors into a coherent multilevel framework of HPV vaccination to inform future intervention development to increase HPV vaccination among adolescents. Factors included in the model are based on the systematic review of twelve reviews representing a broad swath of the literature related to HPV vaccine series initiation and completion. Most factors were consistently identified in multiple reviews, and reviews focused equally on modifiable factors, such as parental knowledge or beliefs, and non-modifiable factors such demographics. Narrowing the scope of the model to individual-, provider-, and clinic-levels allows intervention developers to identify proximal modifiable factors related to vaccination behaviors and to intervene on those factors rather than more distal influences such as community or policy-level factors. The model illustrates the importance of each level as it relates to vaccination for both males and females. It also highlights the relation between levels such as the relation between the clinic- and provider-levels.

Unlike previous models of HPV vaccination,[24,16,18,25] we include factors associated with both adolescent males and females and series initiation and completion in a single model. We chose to incorporate all factors into one multilevel framework to provide a concise visual of the multitude of factors correlated with and predicting HPV vaccination outcomes among all adolescents. Only one review focused exclusively on adolescent males[44] although males were

included in five additional reviews.[41,15,43,14,46] Reviews including both males and females did not always distinguish between those factors associated with vaccination among males versus females which limited our ability to label factors by sex. A future review that compares factors associated with vaccination among males and females using primary studies is needed and can help elucidate differences, if any, between the sexes. Similarly, we chose not to separate the multilevel framework by factors associated with HPV vaccine series initiation and completion. Future reviews that identify the differences between factors associated with initiation and completion can further inform our multilevel framework.

The framework differs from previous models of HPV vaccination[18,27] by identifying correlates of vaccination outcomes as opposed to acceptance of the HPV vaccine and willingness to vaccinate. The model serves as an update to the Fernandez et al. model which presented a multilevel framework incorporating acceptance and willingness research conducted prior to the availability of adequate outcomes research.[18] While acceptance is predictive of vaccination, the previous review was unable to link factors associated with and predictive of vaccination with actual outcomes. This review does link the factors with outcomes, and therefore provides better evidence of the association of these factors with vaccination and more precise targets for intervention. Changes in HPV vaccine recommendations to include males and research on predictors of HPV vaccine initiation and series completion (instead of only acceptance and willingness) also pointed to the need for an updated framework.[51–54] Additionally, the updated model focuses only on vaccination among 9-17 year olds since factors related to parents' decisions to vaccinate their children may differ from young adults' (18 years or older) decisions to self-vaccinate.

Our multilevel framework is meant to inform future intervention development to increase HPV vaccination. If read from right to left, the multilevel framework funnels from the larger health related goal (a reduction of HPV-related diseases) to specific factors influencing the behavior (HPV vaccination) that can lead to that goal. The model highlights for program planners and interventionists specific factors on which to potentially intervene. To build interventions based on the model, planners would continue to work from right to left building out the model to include objectives, methods, practical applications, implementation strategies, and resources as described by Bartholomew Eldredge et al.[55]

Further research is needed for some psychosocial factors included in the model. We found only one review citing parental intentions to vaccinate as an important factor related to HPV vaccine initiation.[44] Many studies examining correlates or predictors of intentions were included in the reviews (see Supplemental Materials for bibliography). However, there is a gap in the research describing the relation between parental intentions and actual vaccination outcomes. Studies in diverse populations often examine correlates of intentions to vaccinate without linking the intentions to series initiation or completion outcomes.[56–59] Additionally, based on theory, intentions may act as a mediator between psychosocial variables and HPV vaccination.[60] This highlights the importance of research that elucidates the relation between intentions, other psychosocial factors, and vaccination outcomes. A clear understanding of the relation can help refine the current multilevel framework of vaccination and inform future intervention development.

Additionally, mixed results exist about the relation between vaccination outcomes and parental knowledge about HPV and the HPV vaccine.[38,40,15,42,20,45] Further research is needed to

understand this relation. However, these findings also highlight the need for interventions that move beyond focusing solely on parental knowledge and providing information. Instead interventions should target knowledge plus other psychosocial factors influencing parents' decisions to vaccinate their adolescent children, including beliefs and attitudes, to create behavior change.[55]

Only one review described psychosocial factors associated with provider recommendation behaviors and HPV vaccination. While studies about provider communication styles and recommendation practices are critical to improving outcomes,[61,17,62] it is also important to understand why providers communicate differentially with parents and differentially recommend the vaccine. Understanding these factors can inform provider-level interventions that can enhance provider communication with parents and vaccine recommendation quality. For example, interventions may focus on improving providers' self-efficacy to recommend the vaccine to a hesitant parent by providing guided practice and feedback opportunities. Additional research on modifiable psychosocial factors can allow for these types of tailored and targeted approaches.

Finally, our systematic review highlighted important implementation strategies at the clinic-level associated with increased HPV vaccination rates. These included provider audit and feedback systems and patient reminder systems. Further research is needed in understanding how these types of systems are adopted and implemented within clinic systems. Implementation science and implementation frameworks can help intervention developers understand the contextual factors in clinics that influence adoption and implementation of these systems.[63]

Limitations

This review has some limitations. First, research not yet incorporated into reviews was not captured in this systematic review. Additional themes or factors may emerge from continued research into factors associated with HPV vaccine series and initiation. Second, clinic-level systems were captured in only two reviews. Some clinic-level best practices for increasing vaccination, such as those described by The Guide to Community Preventive Services (The Community Guide),[64] were not included in this systematic review. While we identified clinic-level practices or interventions associated with increased vaccination, this review was not specifically focused on interventions thus limiting our ability to potentially capture some Community Guide best practices. Limiting the search to only HPV vaccination may have impacted our ability to identify best practices related to improving vaccination outcomes in general. Next, we chose to include all AMSTAR quality reviews and all reviews despite primary studies overlapping to create the multilevel framework of HPV vaccination. Despite our conclusions that there were no significant reasons to exclude reviews based on these criteria, placing restrictions on AMSTAR quality and number of overlapping primary studies between the reviews may have impacted factors included in the model. AMSTAR quality assessments revealed that only five reviews included gray literature searches. This points to the potential for publication bias in these reviews which may have influenced the factors incorporated into the models. Finally, the search periods of the reviews are a limitation. Most reviews were conducted prior to 2011, which fails to capture much research about adolescent males and vaccination. Additionally, factors associated with vaccination may become more or less important over time.

However, we chose not to weigh factors found in more recent reviews over factors found in older reviews.

Conclusion

Adolescent HPV vaccination falls short of national goals and multilevel interventions targeting individuals, providers, and clinics are needed to improve vaccination rates. We found evidence suggesting interventions focused on specific parental psychosocial factors, parental behaviors, provider psychosocial factors, provider behaviors, and implementation of specific clinic systems can improve vaccination among adolescents. We incorporated these factors into a single multilevel framework to illustrate the relations between the factors and levels to inform future intervention development. Future research is needed particularly to examine the relation between parental intentions to vaccinate, provider psychosocial factors influencing behaviors, and clinic-level systems impacting HPV vaccination.

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Figure 1.1 PRISMA Flow Diagram

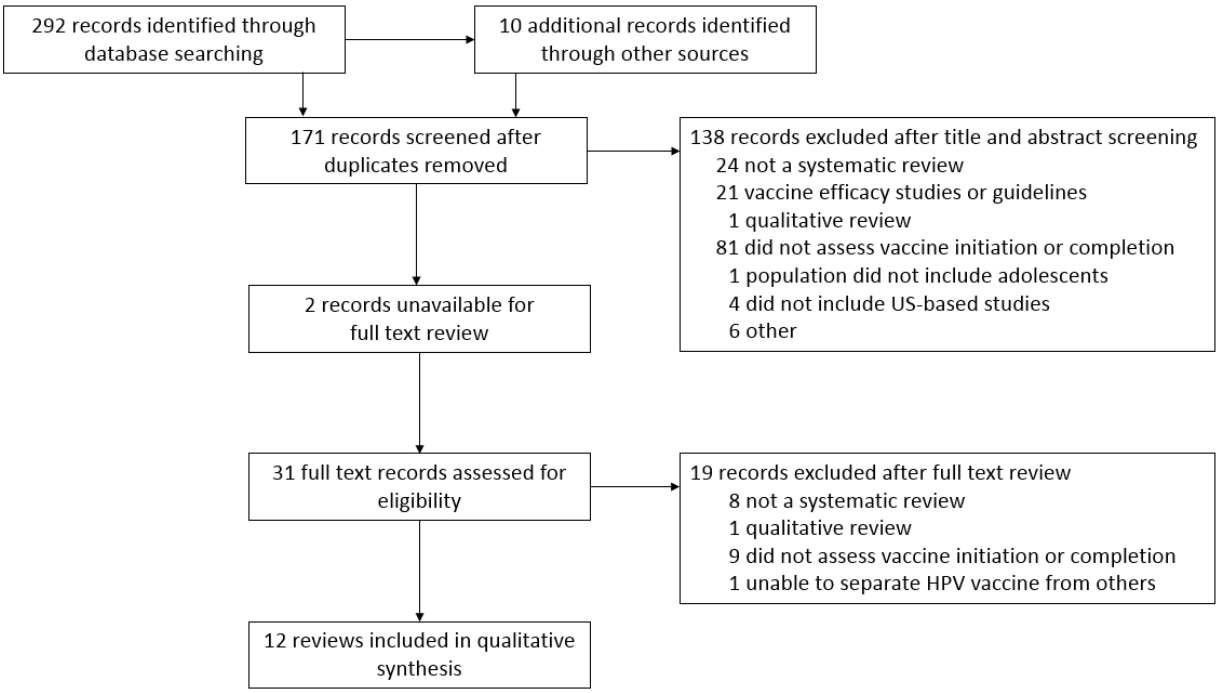

Figure 1.2 Multilevel framework of adolescent HPV vaccination

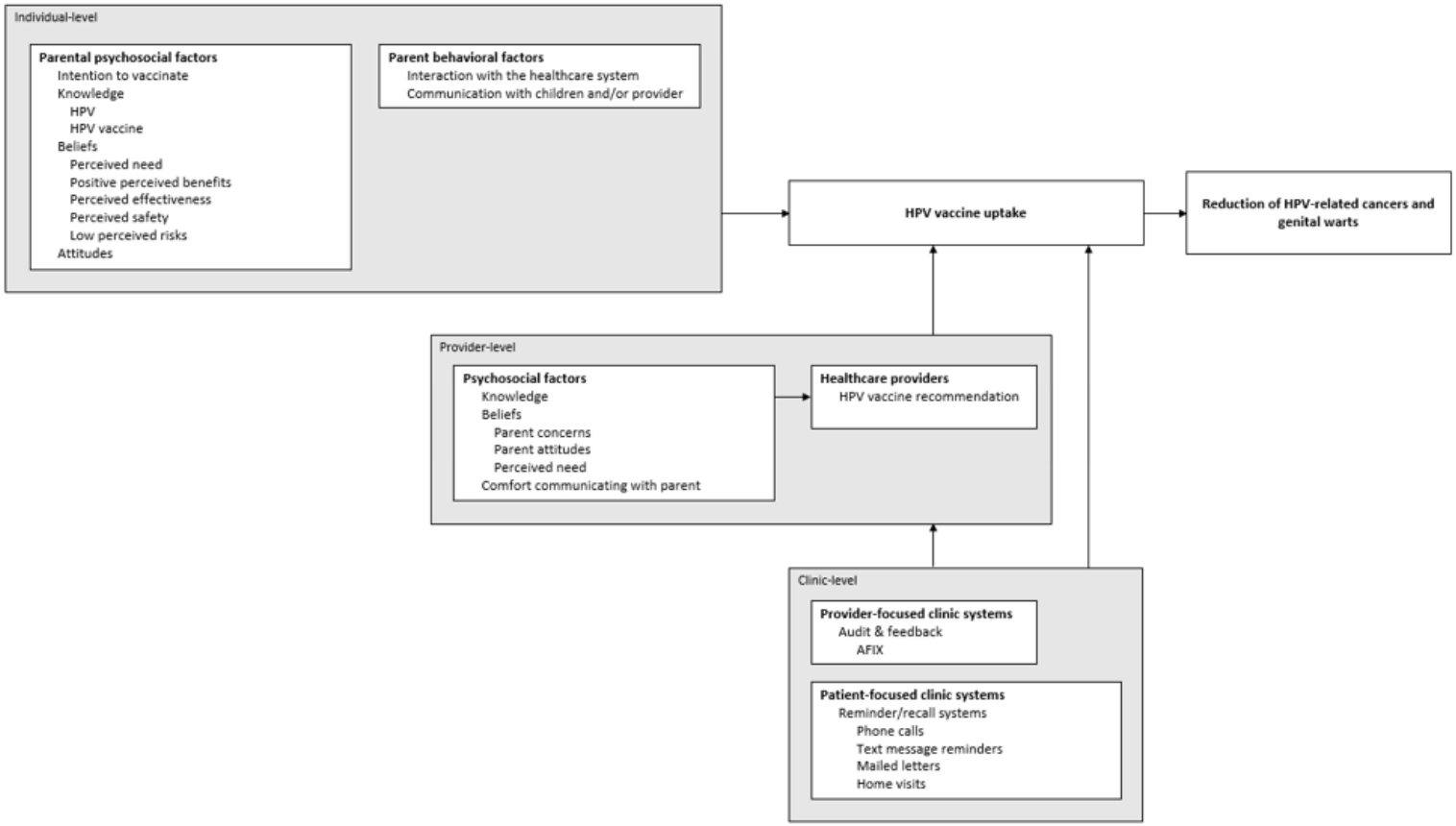

Table 1.1 Review characteristics

Review	Search time period	# of studies (k) & study designs	Populations & country	Factors assessed	AMSTAR score
Bartlett (2011)	2006-Dec 30, 2010	k=14 studies Retrospective cohort, prospective cohort, randomized retrospective cohort, mixed methods	Population: females ages 9-18 years Setting: All U.S.	Outcome variable: HPV vaccine initiation Independent variables: Provider recommendations; parents' knowledge, perceptions, and attitudes (maternal personal experiences, parental concerns related to sexual connotation, parental concerns related to vaccine safety and efficacy); health care services (location to obtain vaccine, obtaining accurate vaccine information)	Low
Fisher (2013)	Database inception-Mar 9, 2012	k=29 publications on 27 studies Cross-sectional, retrospective chart reviews, prospective cohort	Population: Females ages 8-18 years Setting: Most U.S. plus Canada, Europe	Outcome variables: HPV vaccine series initiation, completion Independent variables: Parent ethnicity, religion and frequency of religious attendance; income or area-level indicators; primary caregiver educational attainment; healthcare insurance coverage	Mid-range
Galbraith (2016)	Database inception – Jan 2015	k=67 studies Cross-sectional; qualitative; mixed methods; longitudinal cohort; intervention tests	Population: Adolescent females with African-American or Latino parents Setting: United States	Outcome variables: HPV attitudes, awareness, barriers, acceptability, knowledge, perceptions of HPV or HPV vaccine; HPV series initiation and/or completion[1] Independent variables: Demographic factors; vaccination history; knowledge and awareness; social support; acculturation; communication; mothers' pap history; norms; provider recommendation	Low

Review	Search time period	# of studies (k) & study designs	Populations & country	Factors assessed	AMSTAR score
Gallagher (2016)	Database inception-Feb 2014	k=61 publications with 48 focused on HPV No study designs mentioned; included only those reporting multivariable analyses or qualitative findings	Population: Adolescents ages 9-19 years Setting: Most U.S. plus Canada, Europe	Outcome variable: Completion of multi-dose vaccine within 1 year follow up[2] Independent variables: Age; race; insurance; gender; socio-economic status; healthcare utilization; mothers vaccine related knowledge; adverse events; risk behavior; concomitant healthcare; access; maternal characteristics; provider/organizational characteristics; provider characteristics	High
Holman (2014)	Jan 1, 2009-Dec 31, 2012	k=55 publications Quantitative, qualitative	Population: Adolescents ages 11-17 years; health care professionals; parents; under-served & disadvantaged populations Setting: United States	Outcome variable: HPV vaccination Independent variables: Barriers among different target groups including: health care professionals, parents, underserved and disadvantaged populations, males; barriers to series completion	Low
Kessels (2012)	2006-Mar 7, 2011	k=33 publications on 25 studies Cross-sectional, longitudinal	Population: Females ages 9-18 years Setting: Most in U.S.	Outcome variables: HPV vaccine series initiation and series completion Independent variables for initiation: race/ethnicity; girls' age, area of residence; parental education level and family income; vaccination history; health care utilization; health insurance status; beliefs, attitudes, and intentions; knowledge; sources and quantity of HPV-information' physician recommendation and specialty Independent variables for completion: race/ethnicity; girls' age, healthcare coverage	Mid-range

Review	Search time period	# of studies (k) & study designs	Populations & country	Factors assessed	AMSTAR score
Niccolai (2015)	Database inception - July 2014	k=14 studies Randomized controlled trials; quasiexperimental studies	Population: adolescent males and females 18 years or younger Setting: United States	Outcome variables: Improved HPV vaccine uptake including initiation and series completion' being up to date, timeliness and/or receiving at least one dose Independent variables: Reminder & recall systems; physician-focused interventions; school-based programs; social marketing approaches	Mid-range
Radisic (2017)	Oct 2009-Jul 10, 2015	k=18 studies Quantitative, qualitative, mixed methods	Population: Adolescent males ages 9-18 years Setting: Most in United States; Canada, Italy, Denmark	Outcome variable: Parental acceptability of HPV vaccine defined as vaccine intention or vaccine initiation[1] Independent variables: Health Belief Model constructs; knowledge and awareness; family characteristics; parent-child dialogue; attitude towards vaccinations in general; beliefs	Mid-range
Small (2014)	Jan 1, 2009-June 1, 2011	k=19 publications Longitudinal, cross-sectional	Population: Females Setting: United States	Outcome variable: HPV vaccine uptake Independent variables: Cost and insurance coverage; provider recommendation; vaccination opportunity; HPV and HPV vaccine knowledge; vaccine safety concerns; HPV risk	Low
Trim (2012)	2001-2011	k=53 studies Cross-sectional	Population: Parents of adolescents Setting: Most in United States; EU, Canada, Asia, New Zealand, Australia	Outcome variable: HPV vaccine uptake and acceptance[1] Independent variables: Knowledge, attitudes, behaviors	Low
Valentino (2016)	NA	NA	Population: Female adolescents and young adults	Outcome variable: HPV vaccine uptake	Low

Review	Search time period	# of studies (k) & study designs	Populations & country	Factors assessed	AMSTAR score
				Independent variables: Barriers to uptake related to parents, patients, providers, finances; facilitators to HPV vaccine uptake	
Walling (2016)	Jan 1, 2006 - Apr 30, 3015	k=51 publications Intervention studies	Population: Males and females between 11-26 years Setting: Most in United States	Outcome variables: HPV vaccine uptake Intervention types: Informational interventions; behavioral interventions; environmental interventions	Mid-range

[1] We extracted data related to HPV vaccine series initiation or completion only and excluded data on other outcome variables.
[2] We extracted data related to HPV vaccination only.

Table 1.2 Individual-, provider-, and clinic-level factors associated with HPV vaccination by review

	Bartlett (2011)	Fisher (2013)	Galbraith (2016)	Gallagher (2016)	Holman (2014)	Kessels (2012)	Niccolai (2015)	Radisic (2017)	Small (2014)	Trim (2012)	Valentino (2016)	Walling (2016)
Demographics												
Sex				✓	✓							
Age			✓	✓	✓							
Race/ethnicity		✓	✓	✓	✓	✓					✓	
Insurance status		✓			✓	✓			✓		✓	
Income		✓	✓		✓	✓					✓	
Parent education		✓		✓								
Parental Psychosocial factors												
Intention								✓				
Knowledge	✓		✓		✓	✓			✓		✓	
Beliefs												
Perceived benefits					✓			✓			✓	
Perceived risks					✓				✓	✓	✓	
Perceived effectiveness			✓								✓	
Perceived safety	✓		✓		✓	✓			✓	✓	✓	
Perceived need	✓				✓					✓	✓	
Attitudes	✓				✓							
Related parental behaviors												
Communication with child								✓				
Interaction with HC system	✓			✓	✓	✓		✓	✓	✓		
Provider-level												
Providers												
Recommendation	✓		✓		✓	✓			✓	✓	✓	
Knowledge					✓							
Perceived need											✓	
Perceived parent attitudes					✓							
Perceived parent concerns					✓							

	Bartlett (2011)	Fisher (2013)	Galbraith (2016)	Gallagher (2016)	Holman (2014)	Kessels (2012)	Niccolai (2015)	Radisic (2017)	Small (2014)	Trim (2012)	Valentino (2016)	Walling (2016)
Attitude towards discussing vaccine											✓	
Clinic-level												
Systems												
Patient-targeted reminders							✓					✓
Provider-targeted interventions												✓

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Supplemental Materials

Medline (Ovid) Search Strategy*

1. vaccines/ or viral vaccines/ or immunization/ or immunization schedule/ or immunization, secondary/ or immunotherapy/ or immunotherapy, active/ or vaccination/ or mass vaccination/ or immunization programs/ or (vaccin* or immuniz* or immunis*).ti,ab,kw,rn.
2. papillomaviridae/ or alphapapillomavirus/ or human papillomavirus 6/ or human papillomavirus 11/ or human papillomavirus 16/ or human papillomavirus 18/ or human papillomavirus 31/ or betapapillomavirus/ or gammapapillomavirus/ or mupapillomavirus/
3. (hpv or papillomavirus or papillomaviridae or alphapapillomavirus or betapapillomavirus or mupapillomavirus or genital warts or epidermodysplasia verruciformis or condyloma*).ti,ab,kw,rn.
4. papillomavirus infections/ or warts/ or condylomata acuminata/ or buschke-lowenstein tumor/ or epidermodysplasia verruciformis/
5. 2 or 3 or 4
6. 1 and 5
7. papillomavirus vaccines/ or human papillomavirus recombinant vaccine quadrivalent, types 6, 11, 16, 18/
8. 6 or 7
9. Guideline Adherence/ or Practice Guideline/ or Practice Guidelines as Topic/
10. (guideline* or national consensus or practice parameter*).ti,ab,kw.
11. Physician's Practice Patterns/
12. Attitude of Health Personnel/
13. School nursing/ or School health services/
14. physicians/ or general practitioners/ or physicians, family/ or physicians, primary care/
15. pediatrics/ or (pediatrician* or pediatric primary care or pediatric general).ti,ab,kw.
16. obstetrics/ or gynecology/ or (obgyn or "ob/gyn").ti,ab,kw.
17. nurses/ or nurse practitioners/ or family nurse practitioners/ or pediatric nurse practitioners/ or nurses, community health/
18. nurse's role/ or physician's role/
19. (healthcare provider* or health care provider* or nurse or nurses or physician or physicians).ti,ab,kw.
20. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. 8 and 20
22. parents/ or fathers/ or mothers/ or single parent/ or single-parent family/

23. grandparents/ or legal guardians/

24. (parent* or father* or mother* or grandparent* or guardian*).ti,ab,kw.

25. 22 or 23 or 24

26. 8 and 25

27. insurance/ or insurance, health/ or insurance, health, reimbursement/ or managed care programs/ or health maintenance organizations/ or medicaid/

28. Health Services Accessibility/ or Health Equity/ or Healthcare Disparities/

29. decision making/ or choice behavior/ or uncertainty/ or judgment/

30. attitude/ or attitude to health/ or health knowledge, attitudes, practice/ or adolescent behavior/ or harm reduction/ or health behavior/ or patient compliance/ or medication adherence/ or patient dropouts/ or treatment refusal/ or "patient acceptance of health care"/

31. sociological factors/ or culture/ or socioeconomic factors/ or poverty/ or poverty areas/ or social class/ or social mobility/

32. (accessibility or disparities or disparity or inequalities or inequality or inequity or inequities or children's health insurance plan or CHIP or schip or medicaid or uninsured or insurance or insured).ti,ab,kw.

33. (acceptance or acceptability or attitude* or belief or beliefs or determinant* or decision making or decisionmaking or evidence based or ebp or compliance or refusal or socioeconomic or poverty or income or education).ti,ab,kw.

34. 27 or 28 or 29 or 30 or 31 or 32 or 33

35. 8 and 34

36. 21 or 26 or 35

37. limit 36 to (english language and yr="2006 - 2017")

38. (37 and exp united states/) or (37 not (exp africa/ or exp asia/ or exp australia/ or exp canada/ or exp europe/ or exp south america/))

39. (((comprehensive* or integrative or systematic*) adj3 (bibliographic* or review* or literature)) or (meta-analy* or metaanaly* or "research synthesis" or ((information or data) adj3 synthesis) or (data adj2 extract*))).ti,ab. or (cinahl or (cochrane adj3 trial*) or embase or medline or psyclit or (psycinfo not "psycinfo database") or pubmed or scopus or "sociological abstracts" or "web of science").ab. or ("cochrane database of systematic reviews" or evidence report technology assessment or evidence report technology assessment summary).jn. or Evidence Report: Technology Assessment*.jn. or ((review adj5 (rationale or evidence)).ti,ab. and review.pt.) or meta-analysis as topic/ or Meta-Analysis.pt.

40. 38 and 39

* Medline (Ovid) search strategy was adapted for Pubmed (NLM), PsychInfo (Ovid), CINAHL (Ebsco), and ERIC (Ebsco)

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JOURNAL ARTICLE 2

Parental psychosocial predictors of HPV vaccine initiation among low income, underinsured Hispanic girls ages 11-17 years

Target Journal: The Journal of Adolescent Health

Abstract

Background. Hispanic women experience a disproportionate burden of cervical cancer morbidity and mortality compared to other race/ethnicities. Increasing HPV vaccination among Hispanic adolescents can help alleviate disparities. Guided by the Integrated Behavioral Model, this study aimed to identify psychosocial predictors among parents associated with HPV vaccine initiation among low-income, underinsured Hispanic adolescent females ages 11-17 years in Texas. We also sought to identify correlates of parental intentions to obtain the vaccine for their daughters.

Methods. We conducted baseline surveys with parents recruited in clinic waiting rooms and obtained electronic medical records 6 months following baseline to assess vaccination status. We conducted mixed effects logistic regression to identify correlates of vaccination intention and predictors of HPV vaccination initiation.

Results. Our sample consisted mostly of mothers with less than a high school education born outside of the US with a household income over $15,000 per year. Most daughters had public or private insurance. Correlates positively associated with HPV vaccination intention included subjective norms related to daughter's doctor (AOR=1.04; 95% CI 1.00-1.07), beliefs about HPV vaccine safety (AOR=1.38; 95% CI 1.07-1.79), and self-efficacy (AOR=2.44; 95% CI 1.55-3.84); higher concerns about side effects was negatively associated with vaccination

(AOR=0.73; 95% CI 0.60-0.89). Intention predicted HPV vaccination (AOR=2.42; 95% CI 1.11-5.25) while concerns about sexual disinhibition decreased the odds of vaccination (AOR=0.66; 95% CI 0.47-0.92). .

Discussion. Our study indicates that various constructs of the IBM measured among parents are associated with HPV vaccination intention and that parental intention and concerns about sexual disinhibition are significant predictors of HPV vaccine initiation among Hispanic girls. Further research is needed to explore the role of intention as a potential mediator between psychosocial variables and vaccination status.

Implications and Contributions

Our study identifies important parental beliefs and attitudes that influence HPV vaccination among Hispanic adolescent females. Our findings with Hispanic parents, primarily mothers, indicate concerns about sexual disinhibition and intentions to vaccinate are significantly associated with HPV vaccine initiation among their adolescent daughters. These findings can inform the development of interventions for Hispanic parents to increase HPV vaccination of their children.

Background

The human papillomavirus (HPV) is the most common sexually transmitted infection among sexually active individuals.[1] Persistent infection with high-risk oncogenic types of the virus can lead to cervical, anal, vulvar, vaginal, and oropharyngeal cancers.[2] Cervical cancer is the most commonly diagnosed HPV-related cancer in women in the United States with a rate of 7.4 cases per 100,000 females, and almost all cervical cancers are attributable to HPV.[3]

Disparities exist in HPV infection prevalence, cervical cancer screening, and cervical cancer morbidity and mortality rates. High-risk types of HPV are more prevalent among women with less than a high school education (38%) compared to those with a high school diploma or more (33% and 27% respectively) and among women living below poverty (40%) compared to those at or above the poverty line (27%).[4] High-risk types are also most prevalent among non-Hispanic black women (40%), followed by Mexican American (31%), as compared to other race/ethnicities (28%), and non-Hispanic white women (27%).[4] Hispanic women are significantly less likely than non-Hispanic women to obtain cervical cancer screening,[5] and Hispanic women experience a significantly disproportionate rate of cervical cancer (9.7 per 100,000) compared to non-Hispanic women (7.1 per 100,000).[3] Cervical cancer mortality rates for Hispanic women are second only to rates for Black women and are higher compared to White, Asian/Pacific Islander, and American Indian/Alaska Native women.[6]

Disparities in screening highlight the importance of preventing initial HPV infection. HPV vaccines, available for 9 to 26 year olds, protect against certain virus types that can lead to HPV-related cancers including cervical cancer. There are three available HPV vaccines, all with multi-dose vaccination schedules. The CDC Advisory Committee on Immunization Practices (ACIP) recommends vaccine series be administered to adolescents ages 11-12 years alongside other routine adolescent vaccines.[7] Healthy People 2020 sets the goal that 80% of adolescents ages 13-15 years complete the HPV vaccine series,[8] but national vaccination coverage falls below this goal. In 2014, 60% of females ages 13-17 years initiated the HPV vaccine series and only 40% completed the series.[9]

Identifying predictors of vaccination can inform interventions for priority groups. Studies have examined parental HPV vaccine knowledge,[10–14] parental beliefs and attitudes towards the vaccine,[15–20] barriers to vaccination,[21–23] intentions to vaccinate,[12] and vaccine series initiation and completion[19,24,25] among Hispanic and low income populations. While Hispanic mothers are more accepting of HPV vaccination compared to other race/ethnicities, specific beliefs, attitudes, and barriers can negatively influence the decision to vaccinate their daughters.[26] These include attitudes about sexual activity, vaccine safety, vaccine efficacy, and perceived severity and susceptibility.[26] These psychosocial predictors of vaccination have often been identified through cross sectional[16,20–23] or qualitative studies.[10,15,17,19] Longitudinal studies to identify psychosocial predictors of vaccination among Hispanics are rare and needed since measuring both psychosocial predictors and vaccination status simultaneously obscures the direction of the relationship.[26] This study aimed to identify longitudinal parental psychosocial predictors of HPV vaccination among low-income, underinsured Hispanic girls ages 11-17 years. Based on the Integrated Behavioral Model, we also sought to identify correlates of parental intentions to obtain the HPV vaccine for their daughters.

Methods

This study uses data from *Por Nuestras Hijas* (PNH) (*For Our Daughters*), a group randomized control trial that tested the effectiveness of two parent education interventions to increase HPV vaccination among Hispanic adolescents in Houston, TX. The University of Texas Health Science Center at Houston and the Harris Health System Institutional Review Boards approved this research.

Setting and participants

Data collection occurred between November 2012 and January 2015. Twenty-nine community clinics were recruited into the study, and participants were recruited from within the twenty-nine clinics. Eligible clinics served predominantly Hispanic patients and participated in the Vaccines for Children (VFC) Program. VFC offers vaccines at no cost for patients who are otherwise unable to pay.[27] Participant eligibility criteria included: 1) parents or guardians of a daughter aged 11-17 years, 2) report daughter had not initiated the HPV vaccine series, and 3) self-identify as Hispanic or Latina/o. If a participant had more than one daughter that met eligibility criteria, we restricted questions to the daughter with the most recent birthday. Most participants were parents of the adolescent, although some were guardians or grandparents. For purposes of this study, we refer to all as parents.

Trained, bilingual data collectors recruited parents in clinic waiting rooms, assessed eligibility, and obtained informed consent. Informed consent included consent to access daughters' medical records to assess HPV vaccination status, including information on vaccine doses and dates. Once parents consented, data collectors administered a computer-assisted in-person baseline survey which captured parent and daughter sociodemographics and measured psychosocial variables corresponding to constructs of the Integrated Behavioral Model. Parents received a $20 gift card for completing the baseline survey.

Theoretical framework

The Integrated Behavioral Model (IBM), an extension of the Theory of Reasoned Action and the Theory of Planned Behavior,[28] provided the theoretical framework for this study (see Supplemental Materials). The IBM and empirical literature influenced the selection of variables

assessed in this study. The IBM describes various constructs influencing health behavior and may be helpful in better understanding factors influencing parental decisions to vaccinate their children. According to the IBM, attitudes, perceived norms, and personal agency predict intention which in turn predicts behavior.

Variables and Data Sources

Primary outcome variable. Vaccination status was measured as a dichotomous variable. We measured HPV vaccination status indicating if a daughter had or had not received at least one dose of HPV vaccine at 6 months after baseline. For participants recruited in HHS clinics, we obtained HPV vaccination verification by directly accessing daughters' medical records in Epic, the electronic medical records software utilized by HHS. For participants recruited in community clinics, we submitted written requests asking for documentation of a daughter's HPV vaccination status. We obtained the series dose and date of vaccination for daughters, or we documented if the daughter had not initiated vaccination. We obtained information from parents about alternative clinics their daughters attended for cases where clinics reported that daughters were not patients or if no records were found in Epic.

Secondary outcome variable. Parental intention was measured at baseline using a 5 point-Likert scale. We dichotomized the scale with "no thought of getting her the vaccine," "think I need to consider getting her the vaccine," and "think I should get her the vaccine, but I am not quite ready" categorized as no intention to obtain the vaccine. We categorized "think I will probably get her the vaccine" and "I am committed to getting her the vaccine" as intention to obtain the vaccine for daughter.

Psychosocial variables. Psychosocial variables from the IBM included: HPV awareness and knowledge; HPV vaccine awareness; behavioral beliefs including concerns related to sexual disinhibition (the belief that HPV vaccination may lead to risky sexual behavior);[29] normative beliefs including perceived social norms, subjective norms related to family, and subjective norms related to daughter's doctor; and self-efficacy to obtain the vaccine for daughter. Additional variables measured included parental perceived susceptibility of daughter to HPV; perceived severity of HPV; beliefs about HPV vaccine safety; and concerns about vaccine side effects and cost. Intention, an IBM construct, was included as a psychosocial variable in all analyses with vaccination status as the outcome.

HPV knowledge was measured through a series of three true/false questions with responses added together to give an overall knowledge score (range 0-3). The self-efficacy scale consisted of six items (α=0.63), and a parent's self-efficacy score was the mean of the six items. Each subjective norms scale consisted of two questions measuring beliefs about whether doctors or family members wanted them to vaccinate and motivation to comply. Responses were multiplied to give an overall subjective norms scale (range 0-25). All other variables consisted of one item each measured on a five-point Likert scale. For example, sexual disinhibition was measured by parental agreement with the statement "If my daughter gets the HPV vaccine, she may think it is okay to have sex." The five-point Likert scale ranged from strongly disagree to strongly agree (see Supplementary Materials for all survey items).

Covariates. We selected covariates based on bivariate analyses and literature supporting the relationship of each of these with HPV initiation. These included: daughter's age, daughter's health insurance status, mother's age, and household income.[23,30,31] Because data were obtained

from a group randomized control trial, we dummy coded study arm to include as a confounding variable in the multivariable models.

Data analysis

We computed descriptive statistics for daughter and participant demographic variables and calculated Pearson correlations between predictors to assess associations. For both outcomes, we used mixed-effects logistic regression to account for participant clustering within clinics when computing unadjusted and adjusted odds ratios. Variables significant at the $p<0.10$ level in bivariate analyses were included in multivariable analyses. We controlled for covariates and study arm in multivariable models. Alpha for multivariable analyses was $p<0.05$. All analyses were run using Stata v.14.[32]

Results

We obtained vaccination status via electronic medical records for 765 daughters of participants (Table 1). Mean age for daughters was 13 years, and most (82%) had some form of public or private insurance. Mean parent age was 39 years, and more than half (59%) reported a household income over $15,000 per year. Most parents were female (98%), reported having less than a 12th grade education (70%), and were born outside of the United States (89%). Most parents (79.4%) had other daughters who were unvaccinated at follow up.

Most predictors were positively correlated with each other (Table 2). Subjective norms related to family, and subjective norms related to the doctor were the most highly correlated variables at $r = 0.39$.

Correlates of parental intention to vaccinate

Unadjusted analysis. In unadjusted analyses, correlates positively associated with parental intention to vaccinate included subjective norms related to family (OR=1.03; 95% CI 1.02-1.05), subjective norms related to daughter's doctor (OR=1.06; 95% CI 1.04-1.08), beliefs about HPV vaccine safety (OR=1.56; 95% CI 1.34-1.82), and self-efficacy (OR=3.07; 95% CI 2.28-4.13) (Table 3). Parents with higher subjective norms related to family and daughters' doctors, beliefs about the vaccine's safety, and self-efficacy to obtain the vaccine for their daughters had higher odds of intending to vaccinate their daughters. Correlates negatively associated with intention included concerns about sexual disinhibition (OR=0.88; 95% CI 0.78-0.99), concerns about side effects (OR=0.77; 95% CI 0.69-0.86), and concerns about cost (OR=0.86; 95% CI 0.78-0.95).

Adjusted analysis. In multivariable analyses, variables positively associated with intention to obtain the vaccine included subjective norms related to daughter's doctor (AOR=1.04; 95% CI 1.00-1.07), beliefs about HPV vaccine safety (AOR=1.38; 95% CI 1.07-1.79), and self-efficacy (AOR=2.44; 95% CI 1.55-3.84). Greater concern about side effects (AOR=0.73; 95% CI 0.60-0.89) was negatively associated with HPV vaccination intention.

Predictors of HPV vaccination within six months

Unadjusted analyses. In unadjusted analyses, subjective norms related to family (OR=1.03; 95% CI 1.01-1.05) and subjective norms related to daughter's doctor (OR=1.03; 95% CI 1.00-1.06) were positively associated with HPV vaccine series initiation within 6 months (Table 4). Parents with higher subjective norms related to both their families and to their daughters' doctors had slightly higher odds of having a vaccinated daughter at 6 months

compared to parents with lower subjective norms. Beliefs about HPV vaccine safety were also positively associated with series initiation (OR=1.22; 95% CI 1.01-1.48). Parents with higher beliefs that the HPV vaccine is safe had 22% higher odds of having a vaccinated daughter at 6 months compared to those with lower beliefs in the vaccine's safety. Self-efficacy to obtain HPV vaccine for daughter was also positively associated with series initiation (OR=1.91; 95% CI 1.33-2.76). Parents with higher self-efficacy to obtain the vaccine had nearly twice the odds of having a vaccinated daughter at 6 months compared to those with lower self-efficacy. Finally, intention to obtain the HPV vaccine for daughter (OR=2.01; 95% CI 1.38-2.92) was positively associated with HPV series initiation. Parents who expressed the intention to obtain the HPV vaccine for their daughters had two times the odds of having a daughter vaccinated within 6 months compared to parents that did not express that intention.

Two variables were negatively associated with HPV vaccine series initiation. Low perceived susceptibility that daughter would have an HPV infection was negatively associated with HPV vaccine initiation within 6 months (OR=0.60; 95% CI 0.4-0.95). Parents who perceived their daughter to be less susceptible to HPV had lower odds of having a vaccinated daughter at 6 months compared to those who thought their daughter had about the same chance or higher change of HPV infection as other girls. Second, parents more concerned about the vaccine's side effects had lower odds of having a vaccinated daughter at 6 months than those who were less concerned about side effects (OR=0.86; 95% CI 0.76-0.97).

Adjusted analyses. After adjusting for covariates, parental concern about sexual disinhibition (AOR=0.66; 95% CI 0.47-0.92) and intention (AOR=2.42; 95% CI 1.11-5.25) were significant predictors of vaccination. Parents who intended to vaccinate had nearly two and a half

times higher odds of having a vaccinated daughter at 6 months compared to those who did not intend to vaccinate their daughters at baseline.

Discussion

Guided by the Integrated Behavioral Model, we aimed to identify parental predictors of HPV vaccine initiation of low income, underinsured Hispanic girls ages 11-17 years. We also identified correlates of parental intentions to obtain the HPV vaccine for their daughters. Our study found that parental subjective norms related to daughter's doctor, beliefs in vaccine safety, and self-efficacy are correlated with intention, and intention predicts HPV vaccine series initiation. Greater concerns about sexual disinhibition were negatively associated with initiation. The relationship between parental intention to vaccinate and HPV vaccine series initiation is in line with theory and previous studies focused on vaccination of adolescent girls. As suggested by the IBM, parental intention predicted HPV vaccine initiation, and previous studies have found intention correlated with HPV vaccine initiation for adolecsent girls.[30,33,34]

Aside from intention, no other variables that significantly predicted series initiation in unadjusted analyses were associated with the outcome in adjusted models. This is despite evidence that attitudes and normative beliefs were predictive of vaccination status in previous longitudinal studies.[34,35] Overlapping variance between the predictors and intention may explain these findings. Subjective norms related to family, subjective norms related to doctor, beliefs about HPV vaccine safety, concerns about side effects, and self-efficacy to obtain the vaccine were significantly correlated with intention as expected based on the IBM. Pearson's *r* ranged from 0.16 to 0.30. Overlapping variances could have obscured variable relationships with the outcome, and intention may have overshadowed other predictors in adjusted analysis.

These variables remain important as potential intervention targets. Adjusted analysis to identify correlates of intention showed the significant associations between intention and subjective norms related to daughter's doctor, beliefs about safety, concerns about side effects and self-efficacy. This anlaysis highlights the importance of these variables in interventions aimed at increasing HPV vaccination as they are associated with higher intentions which predicts series initiation. Additional intervention targets include variables which were predictive of series initiation in unadjusted analyses but were nonsignificant in adjusted analysis due to overlapping variance with intention.

This study also found that parents expressing concerns about sexual disinhibition had lower odds of having a vaccinated daughter at 6 months. Findings related to beliefs about the vaccine leading to sexual disinhibition are mixed in previous research. Hispanic parents have previously expressed concerns that obtaining the vaccine for their daughter could lead their daughters to think it is okay to have premarital sex or to initiate sex early.[17,26] A previous study examining HPV vaccine uptake among Hispanic adolescent girls found parental concerns about sexual disinhibition to be the only psychosocial factor associated with uptake.[20] However, parents also see the vaccine as an opportunity to protect daughters who may be sexually active.[36] Research indicates there is no link between HPV vaccination, early sexual debut, or risky sexual behaviors.[37,38] Because this is a concern for Hispanic parents, interventions targeting Hispanic parents should address sexual disinhibiton concerns and highlight research indicating there is no link between vaccination and sexul debut or risky behaviors.

Based on our findings, interventions to increase series initiation among Hispanic adolescent females should tailor content based on Hispanic parents' beliefs about sexual

disinhibition to address these concerns and to provide accurate information. Interveneing on these concerns can help move the conversation about the HPV vaccine from one relating the vaccine to sex to a conversation that reiterates the vaccine is a safe and effective cancer prevention strategy.

Strengths and Limitations

Study strengths include our longitudinal study design and large sample size (N=765). While obtaining vaccination statuses via EMR posed some limitations as noted below, our outcome measure is also a strength. Relying on EMR vaccination status provided accurate initiation data while methods such as parent reporting can lead to underestimation, particularly for girls who are nonwhite race/ethnicity, have a lower household income, have a mother with a low level of education, and have public insurance.[39,40]

This study has some limitations. parents gave the name of clinics their daughters attended for care, and we obtained HPV vaccination status via EMR records at the reported clinics. If a clinic informed us that there was no record of the patient, we attempted to obtain alternate clinic informaiton from parents. We were able to obtain clinic records for most but not all daughters. This limits generalizability since we included only participants whose daughter's vaccination status could be obtained from the EMR. Those who may not regularly access the same clinic or who attend a number of clinics for care were less likely to be retained in the analytic sample. Another limitation is that our data on vaccination status may not have captured those who were vaccianted at alternative locations such as mobile clinics, community vaccination events, or pharmacy clinics thus potentially underestimating vaccination. Finally, outcome measurement at

6 months is a limitation. We did not capture participants who may have vaccinated after the 6 month cutoff, thus again potentally underestimating vaccination initiation.

All predictor variables, including intention, were measured simultanesously at baseline. This limits our ability to assess intention as a mediator between these predictor variables and vaccination status. Our study shows that several of the psychosocial constructs predicted intention and that intention in turn predicted HPV vaccination. This provides some evidence consistent with a mediation hypothesis, and our findings warrant further research using logitudinal measures of intention prior to assessing vaccination and using other analytic methods such as path analysis or bootstrapping.

Conclusion

Identifying correlates of intention and predictors of series initiation can inform future intervention development to increase HPV vaccination among Hispanic adolescents. Overall, intention and concerns about sexual disinhibition are significant predictors of HPV vaccine initiation among low income, Hispanic girls ages 11-17 years. Additionally, variables associated with parental intentions to vaccinate include subjective norms related to daughter's doctor, beliefs about the safety of the HPV vaccine, and self-efficacy. Interventions that focus on these factors may increase intention and ultimately increase HPV vaccine series initiation in this population. Additionally, interventions addressing concerns about sexual disibnhibtion are needed. Interventions that increase HPV vaccination among this population can help reduce later cervical cancer morbidity and mortality and reduce cancer-related health disparities.

Acknowledgements

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Table 2.1 Daughter and participant demographics (N=765)

Variable	n (%) or μ(SD)
Daughter characteristics	
Age, μ(SD)	13.18 (1.97)
Insurance status	
Uninsured	136 (18.06)
Public, private, other insurance	617 (81.94)
Participant characteristics	
Sex	
Female	753 (98.43)
Male	12 (1.57)
Age, μ(SD)	38.79 (6.65)
Education level	
None – 11th grade	530 (69.83)
12th grade - > HS	229 (30.17)
Born in United States	
Yes	81 (10.66)
No	679 (89.34)
Household income	
No income - $14,999	212 (41.25)
$15,000 +	302 (58.75)

Table 2.2 Correlation matrix of predictors

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.
1. HPV awareness	1.00															
2. HPV knowledge	0.14**	1.00														
3. Perceived susceptibility	-0.01	0.13**	1.00													
4. Perceived severity	0.09*	0.11*	-0.03	1.00												
5. HPV vaccine awareness	0.48**	0.02	-0.03	0.06	1.00											
6. Perceived norms	0.06	0.16**	0.03	0.05	0.04	1.00										
7. Subjective norms (family)	0.04	0.08	-0.03	0.02	0.02	0.31**	1.00									
8. Subjective norms (doc)	-0.05	0.09	0.00	0.00	0.05	0.20**	0.39**	1.00								
9. Belief – vaccine safety	-0.01	0.16**	-0.02	0.08*	0.02	0.14**	0.25**	0.25**	1.00							
10. Concern-sexual disinhibition	0.01	0.04	0.05	0.04	0.03	0.01	0.05	0.01	0.05	1.00						
11. Concern – side effects	0.01	-0.04	0.00	0.05	-0.04	0.05	-0.11**	-0.15**	-0.20**	0.08*	1.00					
12. Concern-cost	-0.02	0.05	0.04	-0.01	-0.09*	0.12**	0.06	0.00	-0.05	0.11**	0.10**	1.00				
13. Self-efficacy	0.03	0.05	-0.11**	0.11**	0.06	0.16**	0.20**	0.26**	0.30**	-0.01	-0.16**	-0.19**	1.00			
14. Attitude – important	0.00	-0.02	-0.06	-0.03	-0.02	0.07	0.02	0.02	0.07	0.00	0.02	0.03	0.04	1.00		
15. Attitude - afraid	-0.05	0.02	0.08*	0.01	-0.06	0.02	-0.04	-0.02	-0.14**	0.04	0.22**	0.11**	-0.12**	-0.12**	1.00	
16. Intention	0.04	0.07	-0.02	0.06	0.07	0.02	0.16**	0.23**	0.23**	-0.08	-0.17**	-0.12**	0.30**	0.03	-0.06	1.00

* $p<0.05$
** $p<0.01$

Table 2.3 Correlates of intention to vaccinate

Variable	Unadjusted OR[1]	95% CI	*p*-value	Adjusted OR[2]	95% CI	*p*-value
HPV awareness						
Yes	1.16	0.86-1.57	0.32			
No	REF					
HPV knowledge	1.22	0.95-1.55	0.11			
Perception of daughter susceptibility to HPV						
Higher or about the same chance as others	REF					
Less chance than others	0.93	0.69-1.25	0.62			
Perceived severity of HPV	1.17	0.98-1.41	0.09			
HPV vaccine awareness						
Yes	1.31	0.98-1.76	0.07			
No	REF					
Perceived norms	1.04	0.92-1.18	0.53			
Subjective norms (family)	**1.03**	**1.02-1.05**	**<0.001**	1.02	0.99-1.05	0.18
Subjective norms (doctor)	**1.06**	**1.04-1.08**	**<0.001**	**1.04**	**1.00-1.07**	**0.02**
Belief - vaccine safety	**1.56**	**1.34-1.82**	**<0.001**	**1.38**	**1.07-1.79**	**0.01**
Concerns						
Sexual disinhibition	**0.88**	**0.78-0.99**	**0.04**	1.01	0.82-1.24	0.92
Side effects	**0.77**	**0.69-0.86**	**<0.001**	**0.73**	**0.60-0.89**	**0.002**
Cost	**0.86**	**0.78-0.95**	**0.002**	0.87	0.73-1.03	0.10
Self-efficacy	**3.07**	**2.28-4.13**	**<0.001**	**2.44**	**1.55-3.84**	**<0.001**
General attitudes about vaccines						
Important to receive all	1.119	0.76-1.86	0.45			
Afraid of vaccines daughter receives	0.93	0.85-1.01	0.08			

[1] Bold indicates variables to be included in multivariable analysis with $p<0.10$

[2] Controlling for daughter age, daughter insurance status, parent age, household income, study arm; bold highlights variables significant at $p<0.05$

Table 2.4 Psychosocial predictors by vaccination status and unadjusted psychosocial predictors associated with HPV vaccine initiation[1]

Variables	Vaccinated (n=158)	Did not vaccinate (n=607)	OR	95% CI	*p*-value
	n(%) or mean(SD)	n(%) or mean(SD)			
Psychosocial predictors					
HPV awareness					
Yes	94 (12.63)	374 (28.76)	0.83	0.57-1.21	0.33
No	62 (8.33)	214 (28.76)	REF		
HPV knowledge, μ (SD)[2]	1.94 (0.77)	2.02 (0.75)	0.88	0.65-1.20	0.42
Perception of daughter susceptibility to HPV					
Higher or about the same chance as others	4 (0.58)	27 (3.91)	REF		
Less chance than others	60 (8.70)	292 (43.32)	**0.65**	**0.44-0.95**	**0.03**
Perceived severity of HPV, μ (SD)	4.75 (0.83)	4.70 (0.78)	1.10	0.86-1.40	0.45
HPV vaccine awareness					
Yes	96 (12.75)	356 (47.28)	1.02	0.70-1.48	0.92
No	61 (8.10)	240 (31.87)	REF		
Perceived norms, μ (SD)	3.89 (1.17)	3.82 (1.22)	1.03	0.87-1.21	0.76
Subjective norms (family), μ (SD)[3]	13.51 (9.77)	10.95 (9.40)	**1.03**	**1.01-1.05**	**0.01**
Subjective norms (doctor), μ (SD)[3]	18.08 (8.24)	16.29 (8.15)	**1.03**	**1.00-1.06**	**0.04**
Belief - vaccine safety μ (SD)	4.05 (1.02)	3.82 (1.08)	**1.22**	**1.01-1.48**	**0.04**
Concerns					
Sexual disinhibition, μ (SD)	1.51 (1.12)	1.74 (1.29)	**0.87**	**0.74-1.02**	**0.09**
Side effects, μ (SD)	3.85 (1.52)	4.15 (1.34)	**0.86**	**0.76-0.97**	**0.02**
Cost, μ (SD)	1.89 (1.45)	2.11 (1.58)	0.92	0.81-1.04	0.16
Self-efficacy, μ (SD)	4.53 (0.52)	4.33 (0.63)	**1.91**	**1.33-2.76**	**0.001**
General attitudes about vaccines					
Important to receive all, μ (SD)	4.98 (0.24)	4.96 (0.35)	1.27	0.63-2.58	0.50
Afraid of vaccines daughter receives, μ (SD)	2.00 (1.57)	2.24 (1.71)	0.91	0.82-1.02	0.12
Intention					
Yes	101 (13.41)	291 (38.65)	**2.01**	**1.38-2.92**	**<0.001**
No	55 (7.30)	306 (4.64)	REF		

[1] Daughter's age, daughter's insurance status, and mother's age all significant at $p<0.05$, results not shown; bold indicates variable included in multivariable analysis

[2] Range 0-3

[3] Range 1-25

Table 2.5 Psychosocial predictors of vaccination status[1]

Variable	AOR	95% CI	*p*-value
Perceived daughter's susceptibility			
More or about the same chance as others	REF		
Less chance than others	0.98	0.50-1.90	0.95
Subjective norms – family	1.03	0.99-1.06	0.19
Subjective norms – doctor	1.00	0.96-1.05	0.90
Belief - vaccine safety	0.88	0.63-1.23	0.46
Concerns			
Sexual disinhibition	**0.66**	**0.47-0.92**	**0.01**
Side effects	0.94	0.76-1.16	0.56
Self-efficacy	1.45	0.78-2.69	0.24
Intention			
Yes	**2.42**	**1.11-5.25**	**0.03**
No	REF		

[1] Controlling for daughter age, daughter insurance status, parent age, household income, and study arm; bold highlights variables significant at $p<0.05$

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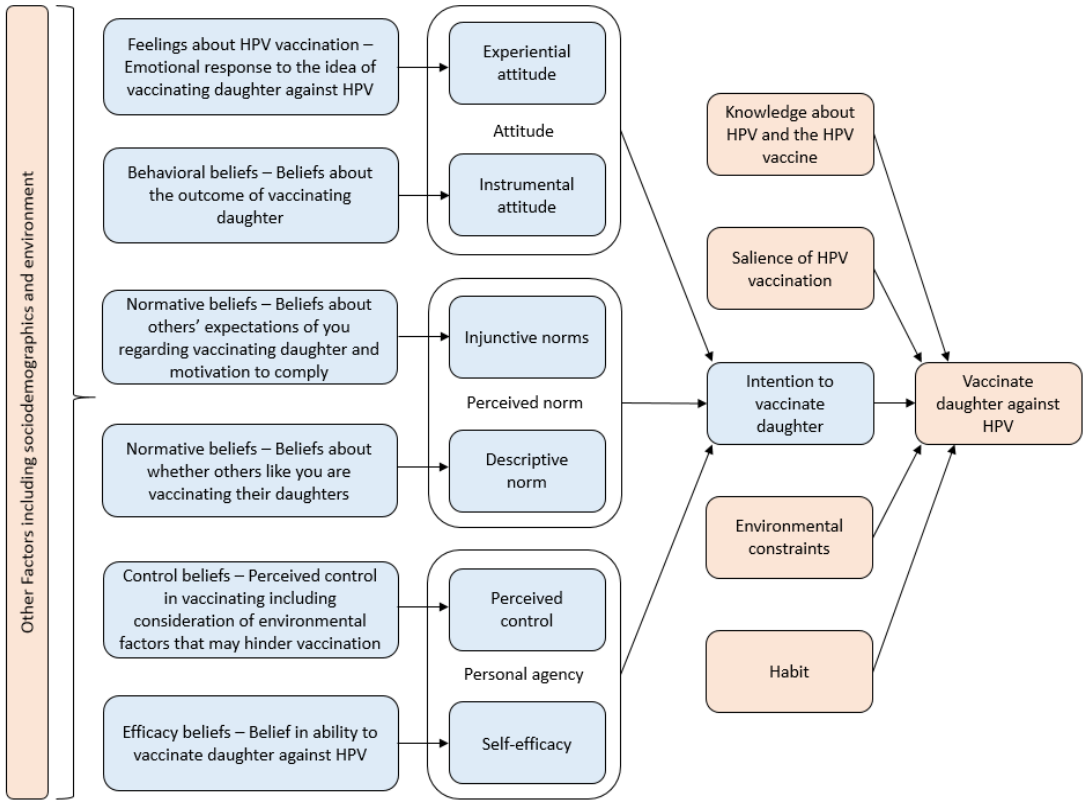
Supplemental Materials

Integrated Behavioral Model



Baseline survey items

Variable	Item(s)	Response Options
HPV awareness		
	Before today, had you ever heard of HPV?	Yes/No
HPV knowledge		
	HPV can cause cervical cancer.	True/False
	HPV can be spread by sexual contact.	
	A woman can usually tell if she has HPV.	
Perceived daughter susceptibility		
	Compared to other girls her age, what do you think the chances are that your daughter will contract HPV?	More chance than other girls About the same as other girls Less chance than other girls
Perceived HPV severity		
	Getting HPV could harm my daughter's health in the future.	5-point Likert Strongly disagree to strongly agree
HPV vaccine awareness		
	Before today, had you ever heard of the HPV vaccine, HPV shot, or cervical cancer vaccine?	Yes/No
Belief about vaccine safety		
	The HPV shot is safe.	5-point Likert Strongly disagree to strongly agree
Concerns		
	If my daughter gets the HPV vaccine, she may think it is okay to have sex.	5-point Likert Strongly disagree to strongly agree
	I worry about the possible side effects of the HPV vaccine.	
	The cost of the HPV vaccine would prevent me from getting it for my daughter.	
Perceived norms		
	Other parents like me are considering getting their daughters the HPV vaccine.	5-point Likert Strongly disagree to strongly agree
Subjective norms - Family		
	My family thinks I should get my daughter vaccinated against HPV.	5-point Likert Strongly disagree to strongly agree
	I want to do what my family members think I should do about getting my daughter vaccinated against HPV.	
Subjective norms - Doctor		
	My doctor thinks I should get my daughter vaccinated against HPV.	
	I want to do what my doctor thinks I should do about getting my daughter the HPV vaccine.	
Self-efficacy (α=0.63)		
	How sure are you that you can request the HPV vaccine for your daughter even if the doctor does not bring it up?	5-point Likert Very unsure to very sure
	How sure are you that you can ask your daughter's doctor questions about the HPV vaccine?	
	How sure are you that you could get the HPV vaccine for your daughter even if you don't have health insurance that covers it?	

	How sure are you that you could get the HPV vaccine for your daughter even if you are worried about the possible side effects? How sure are you that you could get the HPV vaccine for your daughter if you decided you wanted to? How sure are you that you could get your daughter all three HPV vaccine shots even though you'd have to come back after one month and against at three months?	
Intention to vaccinate		
	Please tell me which statement is closest to where you are now in your plans to get your daughter the HPV vaccine.	No thought of getting her the vaccine. Think I need to consider getting her the vaccine. Think I should get her the vaccine, but I am not quite ready. Think I will probably get her the vaccine. Committed to getting her the vaccine.

JOURNAL ARTICLE 3

Clinic Characteristics and Consolidated Framework for Implementation Research Inner-Setting Factors Associated with Implementation of HPV Vaccination Recommendations in a Pediatric Clinic Network

Target Journal: Implementation Science

Abstract

Background. Despite HPV vaccine recommendation guidelines, clinics continue to have vaccination rates lower that national goals. Implementation science frameworks can help identify factors associated with implementation, or lack of implementation, of these guidelines. This study explores the relationship of four Consolidated Framework for Implementation Research (CFIR) Inner Setting constructs, culture, leadership engagement, learning climate, and available resources, with HPV vaccine series initiation among adolescents aged 11-17 years in a pediatric clinic network.

Methods. We recruited providers, staff, and managers from clinics in a pediatric network to complete a survey assessing culture, leadership engagement, learning climate, and available resources at their clinics. We obtained the proportion of eligible patients initiating the HPV vaccine series within the study period for each clinic. We conducted linear regression to identify correlations between CFIR constructs and the proportion of eligible patients initiating the HPV vaccine series.

Results. Five hundred and forty clinic providers, staff members, and managers completed the survey. The mean proportion of eligible adolescents initiating the HPV vaccine series was

56% for all clinics. Leadership engagement was the only CFIR variable significantly related to HPV vaccine series initiation among eligible patients (β=0.30).

Conclusion. Leadership engagement is an important clinic contextual factor associated with HPV vaccine series initiation among clinic patient populations. Further research is needed to identify the causal relationship between these two variables and to identify specific leadership traits that lead to high leadership engagement.

Background

HPV is a common sexually transmitted infection, and persistent infection with specific types of the virus can lead to anogenital cancers and to genital warts.[1,2] The HPV vaccine can protect against specific types of the virus that can lead to these negative health outcomes. Guidelines set by the Advisory Committee for Immunization Practices (ACIP) recommend the HPV vaccine for adolescents and young adults aged 9-26 years.[3] Successful implementation of these guidelines requires appropriate clinic-level processes and systems, leadership support, and buy-in from individual providers.

Although HPV vaccination guidelines exist, vaccination rates are lower than national goals,[4] and clinics have been slow to vaccinate all eligible patients.[5] Adoption and implementation of guidelines, such as those that recommend HPV vaccination for all eligible patients requires buy-in from multiple individuals working within a specific clinical context.[6] Individuals may include providers, clinic administrators, and clinic staff all working together within a clinic that has unique characteristics that can influence adoption and implementation outcomes. Clinic-level characteristics that can hinder implementation of EBIs include competing demands within the clinic, limited resources, limited organizational support, or other practices

that work against or fail to incorporate the new practices.[6,7] Understanding these factors and intervening to facilitate implementation of recommended prevention guidelines fully benefit population health.[8]

Implementation science models and frameworks, such as the Consolidated Framework for Implementation Research (CFIR), offer structure for understanding clinic-level characteristics that may support or impede implementation efforts. CFIR pulls together 39 constructs from 19 implementation science theories, models, and frameworks providing an overarching typology of factors that can influence implementation outcomes.[9] CFIR constructs are organized into five domains with the Inner Setting domain most pertinent to understanding clinic-level factors that may influence adoption and implementation outcomes. Inner setting constructs include structural characteristics, networks and communications, culture, implementation climate, and readiness for implementation.

Inner setting constructs have been linked to implementation of cancer control and prevention EBIs in healthcare settings in qualitative studies.[10–14] However, few studies have examined the relationship between inner setting constructs and cancer control implementation.[15,16] This study aims to identify clinic characteristics and inner setting constructs correlated with implementation of HPV vaccination guidelines within a pediatric clinic network.

This study explores the relationship of four CFIR inner setting constructs: culture, leadership engagement, learning climate, and available resources, with implementation of HPV vaccine guidelines. Previous qualitative research has linked leadership engagement, such as vision setting and enthusiasm for an intervention, with implementation of cancer control and prevention interventions in clinic setting.[16] A better understanding of these clinic contextual

factors related to implementation of vaccine guidelines can inform future interventions by identifying modifiable factors intervention developers and implementation scientists can target to improve compliance with HPV vaccination guidelines.

Methods

This study uses cross-sectional data collected as part of an ongoing randomized controlled trial within a pediatric clinic network located in Houston, TX. Patient-level data were collected July 2014 to June 2015. During that time, the network served 100,263 unduplicated patients aged 11-17 years. Baseline provider and staff data were collected July 215 to January 2016. The University of Texas Health Science Center at Houston Institutional Review Board approved the study.

Participants

Clinic network managers, staff, and physicians seeing patients aged 11-17 years were eligible to participate in an online survey assessing baseline characteristics prior to participating in the randomized controlled trial. To recruit physicians, the clinic network Chief Medical Officer emailed potential participants a brief introduction to the study, an invitation to participate, and a link to the online survey. Clinic managers received an introductory email and survey link from study staff inviting him/her to participate. The email also included a list of all eligible clinic staff invited to participate. Completion of the survey indicated consent to participate in the study. Physicians received $50 gift cards for participation. Clinic managers and staff members received $40 gift cards.

Outcome variable

The outcome variable is the proportion of HPV vaccine-eligible patients initiating the HPV vaccine series from July 1, 2014 to June 30, 2015 in each clinic (n=50). The proportion is calculated as the number of adolescents aged 11-17 years initiating the HPV vaccine series over the number of adolescents aged 11-17 years that visited a clinic during the measurement period. If an adolescent visited a clinic more than once within the measurement period, he or she is counted only once. Patient vaccination status was extracted from the clinic network's electronic medical records system.

Independent variables

Clinic characteristics. We measured clinic characteristics potentially associated with implementation of HPV vaccination guidelines. These included adolescent patient load during measurement period,[17] proportion of White, African American, and Hispanic adolescent patients,[17,18] and proportion of adolescent patients with public insurance.[17,19] All clinic characteristic variables were continuous.

CFIR constructs. Survey items (Table 1) measuring CFIR inner setting variables were adapted from Fernandez et al.,[20] which validated items based on a nationwide survey of providers and clinic staff from 78 Federally Qualified Health Centers.

CFIR inner setting variables included culture, learning climate, leadership engagement, and available resources. Culture is defined as the norms, values, and basic assumptions of a given organization.[9] The culture scale consisted of 7 items. Learning climate is a climate in which 1) leaders express their own fallibility and need for team members' assistance and input, 2) team members feel that they are essential, valued, and knowledgeable partners in the change

process, 3) individuals feel psychologically safe to try new methods, and 4) there is sufficient time and space for reflective thinking and evaluation. Learning climate is a subconstruct of implementation climate, which the survey did not fully measure. The learning climate scale consisted of 5 items. Leadership engagement is the commitment, involvement, and accountability of a leaders and managers in a clinic.[9] It is a subconstruct of readiness for implementation. The leadership engagement scale consisted of four items. Available resources refers to the level of resources dedicated for implementation and on-going operations.[9] It is also a subconstruct of readiness for implementation. The available resources scale consisted of 3 items. We conducted confirmatory factor analyses and examined discriminate validity and inter-item consistency for all four scales (manuscript in development).

Fernandez et al. demonstrated that individual level data collected from providers and staff could be aggregated to the clinic-level when examining inner setting constructs.[20] We validated the Fernandez et al. finding by also calculating inter-rater agreement and examining intraclass correlation values (manuscript in development). Therefore, we were able to combine individual-level data to describe clinic-level inner setting characteristics. We obtained the clinic-level score for each construct based on responses from all participants within each clinic. For example, we summed responses to all items related to culture from X number of participants at Clinic A and calculated the mean. The mean was then the culture score for Clinic A.

Data Analysis

Descriptive statistics were computed for independent variables and participant characteristics. Participant characteristics were not used in analyses for clinic-level outcomes; they are presented for descriptive purposes only to describe the sample completing the baseline

surveys. Participant characteristics include sex, age, ethnicity, clinic role (i.e., clinic staff member, clinic manager, or provider), number of years in practice (for providers), and number of years working in the clinic (for clinic managers and staff). We used linear regression to identify bivariate associations between clinic characteristic variables, inner setting constructs, and the proportion of eligible patients initiating the HPV vaccine series.

We were unable to conduct multivariable analysis due to multicollinearity between CFIR independent variables. High correlations between these variables (Table 2) violates one of the assumptions of multiple regression assuming independence between the independent variables. Including these variables that are highly correlated could lead to inaccurate coefficient estimates.

Results

Participants

Two hundred and twenty-six physicians were invited to participate with 130 completing the surveys (58% response rate). Fifty clinic managers were invited to participate in the study, and 44 completed the baseline survey (87% response rate). Most clinic staff members invited to participate completed the survey with 423 clinic staff members invited and 366 completing the survey (87% response rate). Overall, a range of 20% to 100% of potential participants at each clinic completed a baseline survey with an average of 11 respondents per clinic. Most participants were male, and the mean age was 40 years (Table 3). The majority of participants were non-Hispanic White or Hispanic. Physicians were in practice about 10 years on average, and clinic staff and managers were in their respective clinics for 6 years.

Clinic compliance with HPV vaccination guidelines

Clinic proportions of eligible patients initiating the HPV vaccine during the measurement period ranged from 31% to 83.5% (μ=56.3; SD=13.7).

Clinic characteristics

Adolescent patient load varied with a range of 358 to 4693 unique patients per year (μ=2088; SD=962). The mean proportion of non-Hispanic White patients (μ=40.99; SD=25.1) was higher than Hispanic patients (μ=27.9; SD=20.8) and African American patients (μ=15.9; SD=16.9) in clinics. About a quarter of all patients seen in clinics had public insurance (μ=25.0; SD=24.3) (Table 4).

In bivariate analyses, all clinic characteristic variables were significantly associated ($p<0.05$) with the proportion of eligible patients initiating the HPV vaccine series (Table 4). Adolescent patient load and the proportion of non-Hispanic White patients in clinics were inversely related to the outcome. As adolescent patient load increased across clinics, the proportion of eligible adolescents initiating the HPV vaccine decreased (β=-0.40). As the proportion of non-Hispanic White patients increased across clinics, HPV vaccination decreased (β=-0.64). Conversely, as the proportion of Hispanic and African American patient populations increased across clinics, HPV vaccine initiation increased (β=0.39 and β=0.54, respectively). Finally, as the proportion of patients with public insurance increased across clinics, the proportion of patients initiating the HPV vaccine series also increased (β=0.65).

CFIR constructs

Among CFIR variables, only leadership engagement was positively associated with the proportion of eligible patients initiating the HPV vaccine series (Table 5). Clinics had higher

proportions of eligible patients in initiating the HPV vaccine series if they reported higher levels of leadership engagement (β=0.30).

Discussion

We aimed to identify clinic-level characteristics and CFIR inner setting variables associated with HPV vaccine guideline adherence in a pediatric clinic network. Guideline adherence was operationalized in this study as the proportion of eligible adolescent patients initiating the HPV vaccine series during the measurement period.

Our study identified leadership engagement as a key factor associated with higher adherence to HPV vaccination guidelines. Previous research shows leadership engagement is a facilitator in intervention and evidence-based practices implementation within clinics.[21–23] Our study is the first that we know to quantitatively assess the associations between CFIR inner setting constructs and HPV guideline adherence within a clinic network. Our findings support previous qualitative research indicating that leadership engagement is important to successful vaccination programs within clinics. Razouki et al.[24] found strong leadership support and engagement as a distinguishing factor among clinics successfully implementing influenza vaccination campaigns in a healthcare system versus those with less successful campaigns. Leadership traits included providing support and resources, role modeling, empowering team members, and creating an environment open to idea generation.[24] Positive leadership traits have also been identified among clinic leaders supportive of evidence-based cancer control intervention implementation; traits include vision setting, enthusiasm, and challenging team members to be creative problem solvers.[16]

We also assessed patient-population clinic characteristics associated with guideline adherence. We found that as adolescent patient load increased within clinics, HPV vaccine series initiation decreased. Our findings differ from previous research examining the association between adolescent patient load and adolescent vaccination. In a study of 91 family medicine and pediatric clinics, Moss et al. [17] found no correlation between adolescent patient load in the clinics and HPV vaccine series initiation and series completion, meningococcal conjugate vaccine administration, or Tdap vaccine administration.

There are a few reasons that may explain our finding that HPV vaccination decreased with increasing adolescent patient load within clinics. In previous research, providers cite perceived and actual lack of time to discuss the HPV vaccine with parents as a barrier to HPV vaccine recommendations.[25–27] Providers often fear that they will need to discuss sexual health issues when introducing the HPV vaccine which may take extra time.[28] Additionally, some choose to discuss the HPV vaccine last when recommending adolescent vaccines.[25] Providers with a higher patient load may not allow themselves the time to recommend the vaccine or may not do so because of a lack of perceived time to have a discussion about the vaccine. This is despite recommendations that providers recommend the HPV vaccine the same way as other adolescent vaccines without singling it out as different,[29] a practice that normalizes the HPV vaccine and can lead to increased HPV vaccine series initiation and completion.[30]

In our study, higher proportions of African America patients, Hispanic patients, and patients with public insurance within clinics were positively associated with HPV vaccine initiation in clinics. These clinic-level findings are consistent with national data which indicate that African American and Hispanic adolescent females and males have higher rates of HPV

vaccine initiation than non-Hispanic White adolescents.[31] We also found a significant negative relationship between the proportions of non-Hispanic White patients at clinics and proportion of patients initiating the HPV vaccine in clinics. Further research is needed to explore vaccine hesitancy in this population and provider communication with non-Hispanic White parents. Finally, research supports the positive relationship we identified between public insurance and HPV vaccine initiation.[32,33] However, having public insurance is associated with being less likely to complete the series when compared to those with public insurance.[34] Future interventions should aim to increase completion rates among adolescents with public insurance.

Study limitations

Limitations of this study include the small sample size of clinics and cross-sectional nature of the design. While we were able to collect data from 50 clinics within the pediatric clinic network, the small sample size of clinics limited our power to conduct multivariable analyses. Small sample size and multicollinearity between variables prevented us from using multiple regression to assess associations while controlling for other variables. The nature of collecting clinic-level data from individuals within the clinics would require a much larger sample size in both individual participants and clinics agreeing to participate in the study. Future research should aim to engage larger clinic networks serving adolescent populations. This would allow for analyses that identified relationships between independent variables and HPV vaccination outcomes while controlling for other significant relationships. Additionally, future studies should employ longitudinal designs to identify casual relationships between clinic inner setting constructs and compliance with HPV vaccine guidelines. Finally, provider recommendations are significantly associated with HPV vaccine series initiation.[35] Our study did

not measure provider recommendation preventing us from identifying associations between recommendation behaviors at the clinic, clinic characteristics, CFIR inner setting constructs, and vaccination outcomes.

Conclusion

Implementation of evidence-based interventions is critical to population health, and implementation of HPV vaccination guidelines represents an opportunity to reduce cancer disparities. Our study identified leadership engagement as an important factor supporting the implementation of HPV vaccination guidelines, measured as the proportion of eligible patients initiating the HPV vaccine series. Future research should examine specific leadership characteristics associated with successful EBI implementation. Further, implementation strategies, or implementation interventions, that seek to have EBIs successfully adopted and implemented in clinic settings should focus on engaging with leadership and obtaining leadership support to facilitate success.

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Table 3.1 CFIR survey items

Construct **Subconstruct**	**Items**
Culture	1. People at all levels openly talk about what is and isn't working. 2. Most people in this clinic are willing to change how they do things in response to feedback from others. 3. Difficult problems are solved through face-to-face discussions. 4. We regularly take time to reflect on how we do things. 5. After trying something new, we take time to think about how it worked. 6. It is hard to get things to change in our clinic. 7. People in this clinic operate as a real team.
Implementation Climate Learning climate	1. We regularly take time to consider ways to improve how we do things. 2. People in our clinic actively seek new ways to improve how we do things. 3. This clinic encourages everyone to share their ideas. 4. This clinic learns from its mistakes. 5. When we experience a problem in the clinic, we make a serious effort to figure out what's really going on.
Readiness for Implementation Leadership Engagement	1. The clinic leadership makes sure that we have the time and space necessary to discuss changes to improve care. 2. Leadership in this clinic creates an environment where things can be accomplished. 3. Clinic leadership promotes an environment that is an enjoyable place to work. 4. Leadership strongly supports clinic change efforts.
Available Resources	1. In general, when there is agreement that change needs to happen in the clinic we have the necessary support in terms of budget or financial resources. 2. In general, when there is agreement that change needs to happen in the clinic we have the necessary support in terms of training. 3. In general, when there is agreement that change needs to happen in the clinic we have the necessary support in terms of staffing.

Table 3.2 CFIR independent variables correlation matrix

	Culture	Leadership engagement	Learning climate	Available resources
Culture	1.00			
Leadership engagement	0.69*	1.00		
Learning climate	0.77*	0.91*	1.00	
Available resources	0.63*	0.62*	0.57*	1.00

* $p<0.01$

Table 3.3 Participant demographics and clinic characteristics

Variable	No. (%)	Mean (SD)
Participant Characteristics		
Clinic role		
Physician	130 (24.07)	-
Clinic staff	366 (67.78)	-
Clinic manager	44 (8.15)	-
Age	-	40.18 (12.68)
Sex		
Female	45 (8.36)	-
Male	493 (91.64)	-
Ethnicity		
Non-Hispanic White	183 (34.01)	-
Non-Hispanic Black	52 (9.67)	-
Hispanic	195 (36.25)	-
Native American or Alaskan Native	2 (0.37)	-
Asian	29 (5.39)	-
Native Hawaiian or Other Pacific Islander	4 (0.74)	-
Other	24 (4.46)	-
Prefer not to answer	49 (9.11)	-
Physician years in practice		9.85 (6.85)
Clinic staff and managers' years in clinic		6.39 (6.99)

Table 3.4 Clinic characteristics and CFIR constructs

Variable	Mean	SD
Clinic Characteristics		
Adolescent patient load	2005.26	1028.04
% non-Hispanic White patients	40.99	25.07
% African American patients	15.85	16.87
% Hispanic patients	27.88	20.81
% patients with public insurance	25.03	24.31
CFIR Variables		
Culture	3.56	0.29
Learning climate	3.94	0.35
Leadership engagement	3.92	0.50
Available resources	3.61	0.35

Table 3.5 Clinic characteristics and CFIR constructs bivariate analyses

Variable	B	SE B	*β*	*t*	*p*-value	r^2
Clinic Characteristics						
Adolescent patient load	-0.01	0.00	-0.40	-2.92	**0.01**	0.16
% White patients	-0.35	0.06	-0.64	-5.84	**<0.01**	0.42
% Hispanic patients	0.35	0.08	0.54	4.41	**<0.01**	0.29
% African-American patients	0.31	0.11	0.39	2.90	**0.01**	0.15
% patients with public insurance	0.36	0.06	0.65	5.84	**<0.01**	0.42
CFIR Constructs						
Culture	10.29	6.76	0.22	1.52	0.13	0.05
Learning climate	8.56	5.47	0.22	1.57	0.12	0.05
Leadership engagement	8.18	3.77	0.30	2.17	**0.04**	0.09
Available resources	8.94	5.42	0.23	1.65	0.11	0.05

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CONCLUSION

This dissertation presented three manuscripts aimed at identifying multilevel factors associated with HPV vaccination among adolescents aged 11-17 years. HPV vaccination falls short of national goals, and by identifying modifiable factors associated with vaccination, intervention planners may build targeted interventions to increase vaccination rates among adolescents.

Manuscript 1 included a systematic review of reviews that informed the development of a multilevel framework of HPV vaccination among adolescents. This systematic review identified parental-, provider-, and clinic-level factors associated with vaccination among adolescent males and females. Specifically, parental knowledge, beliefs, attitudes, intentions, interactions with the healthcare system, and communication with their adolescent were associated with vaccination. Provider recommendation of the HPV vaccination was critical to vaccination along with provider beliefs and knowledge about the vaccine. Finally, clinic level systems including provider audit and feedback and patient reminders were associated with HPV vaccination among adolescents. The multilevel framework highlights potential targets for multilevel interventions aimed at increasing vaccination among adolescent populations. Future research at the clinic-level is needed to understand successful adoption and implementation of the clinic-level systems shown to be effective in increasing HPV vaccine series initiation and completion.

Manuscript 2 focuses on parental psychosocial factors predicting HPV vaccine series initiation among Hispanic adolescent females. Additionally, the manuscript describes correlates of parental intentions to obtain the HPV vaccine for their daughters. Increasing HPV vaccination among this population is critical to reducing later cervical cancer disparities. This study

identified parental intentions to vaccinate as an important predictor of HPV vaccine series initiation among Hispanic adolescent females. Parental concerns about sexual disinhibition were also a significant predictor of vaccination status. Correlates of intention included concerns about vaccine side effects, beliefs about vaccine safety, subjective norms related to daughter's doctor, and self-efficacy to obtain the vaccine for daughter. These findings are consistent with the Integrated Behavioral Model which theorizes that attitudes, perceived norms, and self-efficacy are related to intention which in turn predicts behavior. Further research is needed to understand the relationship between these psychosocial factors and parental intentions to vaccinate. While the current study is consistent with a mediation hypothesis, further research is also needed to understand causal relationships between beleifs, norms, self-efficacy and intentions. Future interventions should focus on increasing parental intention and decreasing parental concerns in order to increase HPV vaccine series initiation among Hispanic adolescents. Parental subjective norms, beliefs about vaccine side effects, concerns about cost, and parental self-efficacy are also potential intervention targets.

Finally, manuscript 3 described clinic-level factors associated with the proportion of eligible adolescents initiating the HPV vaccine series with one year. Clinic factors such as the proportions of each race/ethnicity attending the clinics and patient load were significantly associated with the proportion of patients initiating the series. Additionally, leadership engagement, an Inner Setting construct from the Consolidated Framework for Implementation Research, was also correlated with the proportion of patients initiating the series. Future research should aim to identify specific leadership traits associated with leadership engagement. Further research is also needed to understand how leadership engagement and other CFIR Inner Setting

constructs may be associated with the adoption and implementation of HPV vaccination recommendation guidelines and other cancer control and prevention guidelines within clinics.

Overall, this dissertation contributes to the body of literature examining factors associated with HPV vaccination among adolescents aged 11-17 years. By understanding these factors, intervention developers can create targeted and tailored interventions to increase HPV vaccination among adolescents which can ultimately reduce the burden of HPV-related cancers among the general population.

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