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Evaluating nurse engagement with and opportunities for human papillomavirus (HPV) vaccine promotion in Montana

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Chapter 1: Research Overview

Thaker Juthika Jayendra, MHA, Summer 2023 Public Health

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1.1 Introduction

Adolescence marks the transition from childhood to adulthood.[1] During this time of dynamic development, timely preventive care can promote development of safe behaviors and healthy habits that follow later in life. Vaccination is regarded as one of the foundations of preventive care among adolescents.[2] The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination of persons aged 11–12 years to protect against several infections including human papillomavirus (HPV);meningococcal disease; tetanus, diphtheria, and pertussis; seasonal influenza; and SARS-CoV-2.[3] Uptake has remained low nationally, despite the mounting evidence underscoring the safety and effectiveness of the HPV vaccine and sustained efforts undertaken by federal and local agencies, health organizations, vaccine researchers, and public health advocates to facilitate HPV vaccine education, promotion, and administration.[4-6] For example, in 2021, 76.9% of 13-17-year olds in the United States received the first dose of the HPV vaccine and 61.7% of 13-17-year olds finished the series and were fully protected.[4]

Numerous studies have noted the strong association between receiving a recommendation from a healthcare provider and parental willingness to vaccinate their children.[7-9] In fact, one study found that about 66% of patients who were not vaccinated with the HPV vaccine reported not receiving a recommendation from their provider.[10] A national survey on providers' knowledge, attitudes, and behaviors revealed that about two-thirds of the survey participants acknowledged that they did not have enough time to educate and counsel parents and patients on the HPV vaccine.[11] Furthermore, over half of surveyed pediatricians and family medicine physicians in Florida reported that at least one other

healthcare professional in their practice discusses (56.1%) or makes the initial recommendation for (54.9%) HPV vaccination.[29] Engaging health providers from varying specialties and disciplines can pass on the responsibility of providing strong vaccine recommendations that historically lay solely on primary care physicians thereby simultaneously expanding the range of avenues through which parents and patients can obtain HPV vaccine-related education.[12]

Nurses regularly interact with patients, families, and community groups for health promotion and health services administration.[13] Due to their close relationship with the community members, nurses are strategically positioned to positively influence health behaviors to achieve desired health outcomes.[14] To date, most research on engagement of health care professionals in HPV vaccine promotion has focused on pediatricians and family medicine physicians.[12,15-18] Fewer studies have targeted other healthcare providers like nurses and medical assistants that often provide the initial vaccine recommendations.[12,19-22] For this dissertation, I employed qualitative and quantitative research methods to identify viable, scalable interventions to engage nurses in improving HPV vaccine uptake in Montana. For my first research aim (Chapter 5), I conducted a state-wide survey of nurses (registered nurses, advance practice registered Nurses, and licensed practical nurses) and medical assistants who are involved in adolescent immunization delivery services and work at healthcare facilities that participate in the federal vaccine for children program. Using a cross-sectional study design for my first research aim, I was able to gain insights into the current adolescent immunization practices in Montana and understand the knowledge, attitudes, and perceptions of Montana nurses and medical assistants employed at diverse clinic settings regarding the HPV vaccine. These study findings have been published in the BMC nursing journal.

While research on immunization services delivery has mainly focused on private clinics, local public health departments have often been overlooked in national efforts to increase adolescent

vaccination rates.[23-25] Public health clinics are especially crucial for reducing the rural-urban disparity in HPV vaccine uptake in the U.S since they are a frequent source of immunization services for rural adolescents.[26] In my second research aim (Chapter 6), through qualitative interviews with public health nurses working in rural health departments of Montana, I identified clinical workflows and best practices that were associated with lower missed opportunities for HPV vaccination at these facilities. I used a positive deviance approach[27] to identify my study sample and analyzed data generated through the qualitative interviews using the Consolidated Framework for Implementation Research constructs.[28]

For my third research aim (Chapter 7), I conducted an ecological analysis to identify county-level sociodemographic and access-to-care factors that were associated with missed opportunities for HPV vaccination in Montana. I used datasets like the American Community Survey, the County Health Rankings Report, the US census Bureau, and Occupational Licensing Bureau to extract Montana specific data on selected predictor variables.[30-32] I used a generalized linear mixed modeling approach to conduct the analyses.[33] Overall, my dissertation findings suggest that designing and implementing multidimensional interventions on provider-, patient-, practice-, policy- levels and will be key to realizing an increase in HPV vaccination among Montana adolescents.

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Chapter 2: Research Abstract

2.1 Abstract

Purpose: Parental vaccine hesitancy is a known driver of suboptimal vaccine uptake in the United States.[1] Even though a study analyzing parental responses in National Immunization Survey-Teen found that HPV vaccine hesitancy has slightly declined (69% in 2010 v/s 63% in 2019) over the years, only about 52.6% of adolescents in Montana had received all the required doses of the HPV vaccine series in 2021.[2,3] Nurses are at the forefront of healthcare provision and possess a unique ability to influence parental vaccine decisions.[5] By listening to and addressing parents' concerns about immunizations, nurses can dispel misinformation and help change parents' perceptions about the risks associated with immunizations.[6] However, lack of research focused on ascertaining vaccine confidence among nurses impedes the development of evidence-based strategies to effectively engage nursing professionals in HPV vaccine promotion in Montana.

Methods: Aim One: I conducted a statewide cross-sectional survey of Montana nurses' and medical assistants' (n=309) working at facilities participating in the Vaccines for Children program to determine their perceptions, practices, and experiences with adolescent immunization services, with a focus on HPV vaccination. *Aim Two:* I conducted qualitative interviews with public health nurses (*n*=21) employed at public health departments with both higher and lower missed opportunities rates for HPV vaccination to isolate patient-, provider-, and clinic-level factors associated with higher or lower HPV vaccine uptake. For Aims 2 and 3, I defined a clinic visit to be a missed opportunity for HPV vaccination, when an adolescent received other recommended vaccines (Tdap, MenACWY, Influenza) but did not receive an HPV vaccine dose during the visit despite being due or overdue to initiate the vaccine series. *Aim Three:* Using immunization data from Montana's immunization

information system, I conducted an ecologic analysis = and used generalized linear mixed modeling to identify county-level sociodemographic and access-to-care factors that were associated with missed opportunities for HPV vaccination across all clinic settings.

Results: Aim One: In the statewide survey, most respondents (92.5%) agreed that it is important to vaccinate adolescents against HPV before they engage in any physical intimacy. About 38.1% of respondents reported that misinformation that parents receive from the internet and social media were major barriers to HPV vaccine uptake. Regarding strategies to improve vaccination rates in Montana, 61.4% nurses and medical assistants identified emphasizing cancer prevention while discussing HPV vaccine as being very effective. *Aim Two*: Qualitative interviews with public health nurses revealed that among all recommended adolescent immunization, nurses faced most parental vaccine hesitancy with the HPV vaccine. A lack of robust reminder/recall systems, quality improvement initiatives, and vaccine recommendation styles influences community HPV vaccination rates. Public health nurses underscored the need to engage adolescents through tailored vaccine messaging, create training opportunities for nurses in effective vaccine conversations, invest in social media campaigns, encourage collaborations with schools and community organizations, and promote HPV vaccination at every patient encounter. *Aim Three:* County level effects of population density, rurality, income inequality ratio, proportions of families receiving public assistance, proportion of American Indians/Alaska Natives, and children in single parent households were significantly associated with missed opportunities for HPV vaccination after adjusting for individual's age group and gender (p-value<0.05). Increases in county-level estimates of rurality were associated with higher odds of experiencing HPV missed opportunities whereas increases in proportions of families receiving public assistance, proportion of American Indians/Alaska Natives, income inequality ratio, children in single

parent households, and population density were associated with lower odds of experiencing missed opportunities for HPV vaccination.

Conclusion: Nurses, along with other health professionals, play a key role in increasing vaccination rates and their contribution toward primary prevention of HPV-related infection is crucial. However, multi-level strategies are required to support the integration of nurses as active HPV vaccine advocates and increase HPV vaccine use in rural and medically underserved areas. The ecologic analysis presented an efficacious way of identifying geographical disparities in HPV vaccine uptake risk, thus helping focus resources on populations in need.

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Chapter 3: Background

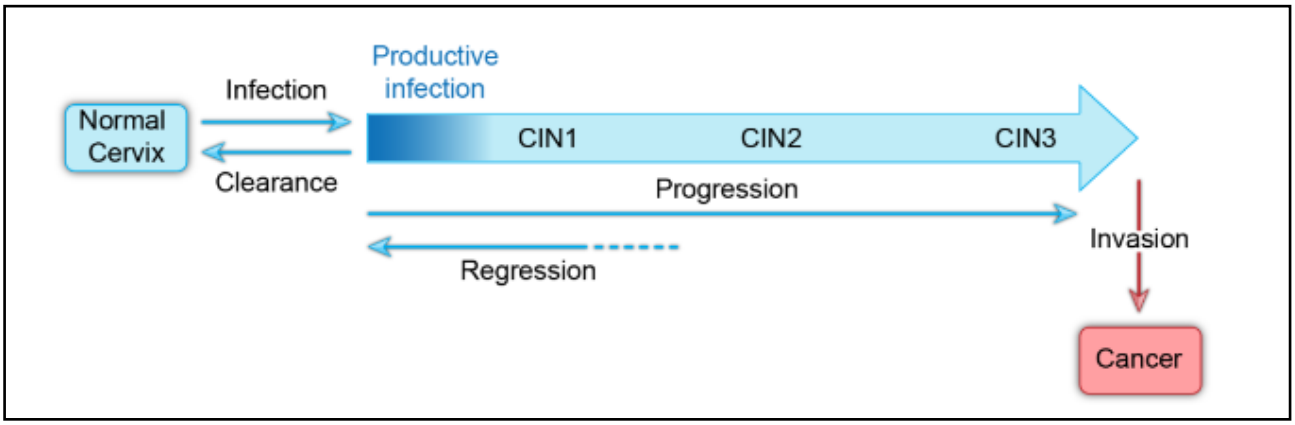
3.1 Human papillomavirus

Human papillomavirus (HPV) is a heterogenous group of viruses divided into 5 different genera: Alpha-papillomavirus (mucosal and skin), Beta-papillomavirus (skin), Gamma-papillomavirus (cutaneous), Nu-papillomavirus (cutaneous), and Mu-papillomavirus (cutaneous) according to DNA sequence homology in the L1 gene.[1] More than 650 distinct animal and human papillomaviruses have been identified and sequenced with over 440 different types that have evolved to exist as human papillomaviruses. Different strains of HPV have specific affinity towards distinct anatomical sites (i.e., skin and mucosa) causing distinctive clinical diseases.[2,3] Specifically, viruses within the Beta, Gamma, Mu, and Nu genera cause pathologies of the cutaneous epithelium, whereas viruses within the Alpha genus infect both cutaneous and mucosal epithelia.[3] These pathologies could include low risk hyperproliferative lesions like cutaneous/mucosal warts or asymptomatic precursor lesions progressing to high-grade neoplasia or malignancies in some instances.[4,5] The mucosal alphaviruses are further classified as high-risk (HR-HPV) and low-risk (LR-HPV) depending on whether they can cause cancer.

The high-risk papillomaviruses play a key role in causing almost all cases of cervical cancer in women and are also highly associated with cancers of the lower genital tract, anus, and oropharynx in both men and women.[6] The HPV virus is transmitted through skin-to-skin contact and the majority of individuals acquire the infection within the first years of sexual activity.[7] The Centers for Disease Control estimates that at least half of all sexually active individuals will acquire HPV at some point in their lives, and at least 80% of women will acquire an HPV infection by age 50.[10] In fact, in a study of US women, 25% of 14-to-19-year-olds and 45% of 20-24-year-olds were infected with at least one HPV type.[91] While the majority of sexually active individuals will contract at least one type of HPV in their lives, most high grade infections are cleared by the immune system within one or two years.

Infections with HPV 16 tend to persist longer and are estimated to clear at an average of 12.2 months.[8,9] However, long-term persistent infection leads to continual expression of viral oncogenic protein abrogates and inhibition of immune detection (Figure 3.1) Consequently, the infected cells over proliferate with accumulation of cellular mutations, leading to the formation of HPV-mediated cancers.[2] 'Low-risk' HPV alphavirus types cause benign anogenital warts and recurrent respiratory papillomatosis and are only rarely found in squamous intraepithelial lesions. The Beta, and gamma-papilloma group of viruses cause asymptomatic lesions of the skin in immunocompetent as well as immunocompromised individuals.[11,12]

Figure 3.1: A model showing the progression of HPV infection to invasive cancer



**CIN: Cervical Intraepithelial Neoplasm*
Adapted from: Della Fera AN, Warburton A, Coursey TL, Khurana S, McBride AA. Persistent human papillomavirus infection. Viruses. 2021;13(2):321 https://www.ncbi.nlm.nih.gov/pubmed/33672465. doi: 10.3390/v13020321

To date, more than 18 anogenital high grade HPVs have been identified, these include HPV types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 69, 73, and 82. Though HPV 16, 18, 31 and 51 are the most prevalent types, the distribution pattern shows diverse regional variation.[13] For example, HPV types 18, 52, and 58 were reported to be more prevalent in Asian populations, types 81, 11 and 16 were the most commonly identified genotypes in Qatari women [15], type 35 among a sample of Nigerian women, and HPV types 16, 18, 45 and 16.52 were prevalent among North American and

European population respectively.[14-16] Studies from multiple countries have also reported co-infection with different HPV types in 20-45% among infected women.[17] High-risk HPV are causally associated with 99% of all cervical, 25% of head and neck, 70% of vaginal, 88% of anal, 43% of vulvar and 50% of penile cancers.[18]

3.2 Burden of HPV-attributable infections

Globally, HPV is the most common oncogenic virus, causing an estimated 5% of the total cancer burden worldwide.[19] Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States, with 13 million new cases emerging every year. About 42 million Americans are currently infected with HPV. A CDC-led analysis of Cancer Statistics data in the U.S. from 2012-2016 estimated that an average of 34,800 HPV-associated cancers were reported each year. The most common were cervical (10,900) and oropharyngeal cancers (13,500) followed by anal (6200), vulvar (2800), penile (800), and vaginal (600) cancers.[18] Overall, annual direct medical costs for HPV-associated diseases in the United States are an estimated $8 billion US dollars, out of which 1 billion dollars are spent on treating HPV-caused cancers. including $6.6 billion (82.3%) for routine cervical cancer screening and follow-up, and $200 million (2.1%) for recurrent respiratory papillomatosis treatment.[20]

Anogenital warts, also referred to as condyloma acuminatum, is the most common clinical expression of an HPV infection. Anogenital warts are benign and are not associated with mortality, but their presence can cause emotional distress among patients due to pain, bleeding, and itching. LR-HPV types 6 and 11 are most commonly associated with anogenital warts. Being highly infectious in nature, research shows that approximately 65% of people with sexual partners that are suffering from anogenital warts will develop warts themselves. Even though anogenital warts are benign in nature, several studies have reported an increased risk of developing cervical precancerous lesions, penile

precancerous lesions, and other anogenital cancers in patients with anogenital warts.[29-31] The global incidence of anogenital warts ranges from 160 to 289 per 100,000 person-years as reported in a systematic review.[22] In the United States, incidence rate is between 100 and 200 new cases per 100,000 general adult population; with rates being highest among women aged 20–24 years and men aged 25–29 years. CDC estimates about one in 100 sexually active adults in the U.S. has genital warts at any given time.[21]Annually, about $300 million dollars are spent to treat anogenital warts in the US. [20] The presence of multiple sexual partners has been identified in multiple studies as an important factor contributing to the increased burden of anogenital wart development. Additionally, having a new sexual partner every in the last 12 months, smoking, and immunosuppression are also associated with an elevated risk of anogenital warts.[23]

Recurrent respiratory papillomatosis (RRP), which is caused exclusively by human papillomavirus (HPV), is a rare condition characterized by recurrent growth of benign papillomata in the respiratory tract. Though benign in nature, RRP could be extremely distressing as the papilloma extend throughout the airway and cause breathing difficulties and tend to recur after surgical removal.[24] A recurrence rate of 71.9% in children and 22.8% in adults leads to the necessity of prolonged surgical interventions for years. Mostly caused by LR-HPV types 6 and 11, HR-HPV types 16 and 18 are rarely detected in the papilloma and can lead to the development of cancers. The incidence rate of RRP is estimated to be 4.3 cases per 100,000 children and 1.8 cases per 100,000 adults.[25] In children, the transmission most commonly occurs during birth if the mother had active warts during pregnancy. The risk of developing cancer is estimated to be 3-7% in adults and less than 1% in children with RRP. The annual estimated costs related to the management of recurrent respiratory papillomatosis in the US is 150 million dollars every year.[27]

Cervical cancer is the fourth most frequent cancer among women and the fourth leading cause of cancer deaths worldwide (second in women aged 15–44 years) with an estimated 570,000 new cases and 311,000 new deaths occurring in 2018.[28] The estimated global age-standardized incidence of cervical cancer was 13·07 per 100 000 women globally and varying widely among countries from less than 2 to 75 per 100 000 women.[28] The American Cancer Society has estimated that in the United States, about 13,960 new cases of invasive cervical cancer will be diagnosed in the year 2023 and 4310 women will die from the disease.[32] HPV type 16 is responsible for 50% of cervical cancer cases, and together with type 18, accounts for 70% of all diagnosed cases. Even though the incidence of cervical cancer has significantly reduced over the past years due to screening, some communities continue to have higher incidence rates of cervical cancer. In the United States, cervical cancer incidence and mortality are higher among some racially marginalized populations, women residing in rural areas, women who lack adequate insurance, and women residing in the Southern region.[33,34] Risk factors for cervical cancer are well-documented and include early onset of sexual activity, multiple sexual partners, smoking, a history of sexually transmitted diseases, and immunosuppression.[32]

Oropharyngeal cancers caused by HPV has been dubbed the fastest growing cancer among middle aged white men (40-59 year old) in the US.[35] Globally, 456,000 head and neck cancer cases are diagnosed and 37,200 cases are attributable to HPV, specifically 29,000 in the oropharynx, 4400 in the oral cavity, and 3800 in the larynx.[19] In the United States, despite observing a decline in the prevalence of tobacco smoking and a 50% reduction of HPV-negative oral cancers, the population-level incidence of HPV-positive oral squamous cell carcinoma increased by 225% from 0.8/100,000 to 3.6/100,000 between 1998-2004.[37] The majority of oropharyngeal infections can be attributed to HR-HPV type 16.[38] Transmission of oral HPV is primarily through sexual contact, with oral-genital contact leading to oral and oropharyngeal infections. Men are 2 to 4 times more likely to develop HPV-associated

oropharyngeal cancer when compared to women.[39] In the US, concomitant oral HPV infections were detected among 10% of women with a pre-existing cervical HPV infections and cytological abnormalities.[36] Chaturvedi et al estimated that by the year 2030, half of all head and neck cancers will be related to HPV, thus calling for immediate attention to promote efforts for addressing the epidemic of HPV-associated oropharyngeal cancers.[40]

Even though HPV-related penile cancers are relatively rare in developed countries with an incidence rate of 1.5 cases per 100,000 people, it is estimated that about 60% of penile cancers diagnosed every year in the United States can be attributed to HPV.[41] Approximately, 1570 cases of penile cancer were reported in the US in 2012 with 310 deaths resulting from penile cancer. Penile cancer is commonly diagnosed in men ages 50-70 years. Incidence of penile cancer in the US is highest among Hispanics, and men who live in the Southern US and areas of high poverty.[45] Risk factors for penile cancer includes age (peak incidence at >60 years of age), HPV infection, smoking, obesity, poor hygiene, inflammatory conditions, early age of sexual intercourse, higher lifetime number of sexual partners, and phimosis.[43] Like other HPV caused high grade carcinomas, HR-HPV 16 accounts for 63% of all HPV-positive cases of penile cancer. Evidence from multiple case control studies have shown that seropositivity with HR-HPV type 16 is as strongly associated with penile cancer as it is with cervical cancer.[44]

Among HPV-related cancers, anal cancers have been linked to HPV with the highest DNA detection rates just after cervical cancer.[46] HPV DNA prevalence has been estimated at 94% in AIN grades 2/3 and 88% in anal cancer, with HPV16 the most frequent HPV type identified. The burden on HPV-associated anal cancers is particularly high among men who have sex with men, anyone with a history of anal warts or high-grade CIN/ VIN/cervical or vulvovaginal cancer; immunosuppressed populations, including those with human immunodeficiency virus (HIV) infection and graft recipients.

For women diagnosed with cervical cancer, the relative risk of developing anal cancer is increased five times as reported in a study using data from the US Surveillance, Epidemiology, and End Results (SEER) program. The incidence of anal cancer increased by 2.0% [APC=2.0%, 95% CI: 1.3%-2.7% between 2009-2017. The age-adjusted rate of new cases of anal cancer was 1.9 per 100,000 men and women per year based on 2016–2020 cases.[32]

Human papillomavirus infection that causes vulvar intraepithelial neoplasia (VIN) is a predisposing factor for vulvar cancers. About 80% of untreated women with VIN stage 3 will develop invasive vulvar cancer. The three most common types of HPV strains associated with vulvar cancer are HR-HPV types 16, 18, and 33.[47] A significantly higher incidence of VIN is reported among white women than among black, Asian/Pacific Islander, or Hispanic women. HPV-associated vulvar cancer often occurs in younger women (35-65 years of age) and about 15% of all cases develop in women under 40 years of age.[48] In the US, the age-adjusted rate of new cases of vulvar cancer was 2.5 per 100,000 women per year and the death rate was 0.6 per 100,000 women per year based on 2016–2020 data.[140] Documented risk factors for HPV-associated vulvar cancer include VIN, past history of sexually transmitted diseases, low economic status, or nicotine abuse.[46]

Persistent HPV infection particularly with HPV type 16 has been associated with long-term development of vaginal precancers and cancers.[5] HPV-caused vaginal cancer is a rare malignancy like vulvar cancer, constituting only 1%–2% of all female genital tract malignancies and only 10% of all vaginal malignant neoplasms. Smoking, immunosuppression, high number of sexual partners, low socioeconomic status, prior hysterectomy, and also history of cervical precancerous and cancerous lesions are known to be risk factors that have been described for vaginal cancers. Past history of cervical cancer is a contributing factor to the development of vaginal cancer as both these anatomical sites share exposure and susceptibility to HPV-related infections.[49] In the United States, about 700

cases of HPV associated vaginal cancers are diagnosed every year. The average age of diagnosis is 67 years. Less than 15% of vaginal cancer cases are diagnosed below the age of 50 years.[50]

3.3 HPV vaccination

The first HPV vaccine was first introduced in 2006 in a quadrivalent formulation. The availability of the HPV vaccine became a powerful tool for prevention of HPV-associated genital infections and precancerous lesions. The HPV vaccine contained noninfectious virus-like particles (VLPs) of the L1 epitope and were administered as a series of 3 injections over a 6-month period (at 0, 2, and 6 months).[51] In the US, quadrivalent vaccine was introduced in 2006 with routine immunization recommended for girls aged 11 or 12 years and catch-up vaccination for females 13–26 years. In 2009, a different bivalent vaccine was licensed and approved for administration. The bivalent vaccine provided protection against high risk HPV strains 16 and 18, which are known to cause 80% of all cervical cancers.[52] When the HPV vaccine was first added to the immunization schedule, it was exclusively recommended for girls to protect against cervical cancer.[53] Studies have identified men as playing a major role in the acquisition and transmission of the HPV virus.[54] Also, with growing evidence supporting the protection offered by the HPV vaccine against oropharyngeal, penile, and anal infections in men, the recommendations were expanded in the year 2011 to include males.[53,55,56]

The quadrivalent vaccine (qHPV) protected against four different strains of the HPV virus including the type 16 and 18 that were known to be a causal agents in the etiopathogenesis of 70% of cervical cancer; anal intraepithelial neoplasms; 50% of cervical intraepithelial neoplasia (CIN) grade 2 lesions; 35% to 50% of all CIN grade 1, vulvar intraepithelial neoplasia (VIN) grade 1, and vaginal intraepithelial neoplasia grade 1; and 90% of genital warts.[56] By the beginning of 2012, HPV vaccination had been introduced into national immunization programs in at least 40 countries.

Australia, the United Kingdom, the United States, and Canada were among the first countries to introduce national HPV vaccination drives.[53] Additionally, GAVI, The Vaccine Alliance, started the first HPV vaccination program in Kenya in 2013, thus vaccinating 300,000 girls and helping seven other countries initiate such programs.[57]

Between December 2014 and June 2015, a new nine valent HPV vaccine (9vHPV) was granted marketing authorization in the USA and Europe.[53] The 9vHPV was developed from the previous quadrivalent HPV vaccine and includes five additional HPV types (6, 11, 16, 18, 31, 33, 45, 52, and 58) that increase the level of protection toward HPV-related cancers.[58] The 9vHPV vaccine protects against seven HR-HPV types that together cause about 90% of cervical cases. On time vaccination of adolescents with the HPV vaccine could prevent up to 90% of cervical cancers and 96% of all anal cancers.[59] Since late 2016, the 9HPV vaccine is the only vaccine type available for administration in the United States. Several professional organizations like the Advisory Committee on Immunization Practices (ACIP), American Cancer Society, the American Academy of Pediatrics and the American Academy of Family Physicians strongly encourage all age-eligible individuals to get vaccinated with recommended doses of the HPV vaccine for optimum protection.[60-62]

Current ACIP guidelines recommend that an adolescent receive the following vaccines: quadrivalent meningococcal conjugate vaccine (MenACWY): 1 dose at 11 to 12 years of age tetanus, diphtheria, and acellular pertussis, absorbed vaccine (Tdap) : 1 dose at 11 to 12 years of age, influenza: 1 dose every year, and human papillomavirus vaccine: 2 doses at 9 through 14 years of age at 0 and 6-12 months, 3 doses for persons 15 through 26 years of age.[60] For HPV vaccine, ACIP also recommends vaccination for everyone through age 26 years if not adequately vaccinated when younger. Vaccination is not routinely recommended for individuals over 27 years of age. However, some adults

ages 27 through 45 years might decide to get the HPV vaccine if they stand to benefit from getting vaccinated as determined through a shared decision making with their providers.[60]

Surveillance studies from multiple countries, including the US, have consistently indicated that the HPV vaccine is safe for administration.[52,63-65] In the United States, patients, healthcare professionals and vaccine manufacturers routinely report incidences of adverse events following the administration of a US licensed vaccine to the Vaccine Adverse Event Reporting System (VAERS).[66] Between 2009-2015, 19,760 adverse event reports following HPV vaccination were reported to VAERS. During this time period, a total of 60 million doses of the qHPV vaccine were administered to boys and girls ages. Out of the 19,760 adverse event reports, approximately 94.2% of the events were non-serious. Out of the 94.2% of non-serious events, dizziness, syncope, and injection site reaction were most commonly reported adverse events.[67] A significant reduction in adverse event reporting rate per 100000 HPV vaccine doses following administration was observed from 2015 to 2018: 44.7 in 2015, 47.1 in 2016, 35.6 in 2017, and 29.4 in 2018.[68] Furthermore, an analysis of data for over 600,000 vaccination records obtained from seven large managed care organizations showed no evidence that administration of the qHPV vaccine is associated with Guillan–Barré Syndrome, stroke, appendicitis, seizures, syncope, allergic reactions, and anaphylaxis.[69,70] Researchers did find a non-statistically significant relative risk (RR) of 1.98 for venous thromboembolism (VTE) following qHPV vaccination among females ages 9–17 years with pre-existing risk factors for VTE.[70] However, in a large scale epidemiologic study from Denmark and Sweden, the researchers found no evidence supporting association between exposure to qHPV vaccine and autoimmune, neurological, as well as venous thromboembolism among a cohort of one million adolescent girls aged 10-17 years.[71] Analysis of data from another safety surveillance system in the US, the Vaccine Safety Datalink, echoed similar findings. The risk of developing venous thromboembolism among 9- to 26-year-olds was not elevated following HPV4 exposure.[72]

Furthermore, epidemiologic evidence of an association between qHPV vaccine and primary ovarian insufficiency causing infertility has not been observed.[52,73] On a global level, the World Health Organization's Advisory Committee on Vaccine Safety reviewed post marketing data from 21 countries and noted the growing evidence on the safety of the HPV vaccine to be assuring. With the exception of syncope, no other adverse events under consideration were found to be causally associated with HPV vaccine exposure.[74]

Since the HPV vaccine was first introduced in national recommended immunization schedules, vaccine research studies have shown that the HPV vaccine is extremely effective at significantly reducing the incidence of HPV-related anogenital warts, cervical intraepithelial neoplasms, and cancers.[79-82,84-86] A meta-analysis of 65 studies focused on estimating the population-level impacts following HPV vaccine administration in 14 high income countries found that countries with more than 50% vaccine coverage showed a 68% reduction in HPV type 16 and 18 infections, and a 61% reduction in anogenital warts among girls 13-19 years of age between pre- and post-vaccination period.[83] Additionally, incidence of anogenital warts reduced significantly in boys younger than 20 years of age by 66% and by 68% in women 20–39 years of age due to effects of herd immunity and cross protection.[83] Vaccination was also associated with a significant decrease in the prevalence of HPV types 31, 33, and 45 infections in 13-19 year old girls and women [RR= 0.46, 95% CI: 0.33-0.66]. A similar trend was observed in young Dutch women where on-time vaccination resulted in significant reductions in incident and prevalence of HPV types 31, 33, 35 and 45 infections.[87]
After the introduction of the HPV immunization program in the UK, the incidence rates of CIN3 and cervical cancer reduced substantially among young women who were vaccinated at an early age.

The estimated relative reduction in cervical cancer rates by age at which the vaccine was offered were 34% for age 16–18 years (school year 12–13), 62% for age 14–16 years (school year 10–11), and

87% for age 12–13 years (school year 8), compared with the reference unvaccinated cohort. The corresponding risk reductions for CIN3 were 39% for those offered at age 16–18 years, 75% for age 14–16 years, and 97% for age 12–13 years. In Australia, another country with high HPV vaccination rates, the incidence rates of genital warts dropped by a staggering 73% among women 12-26 years of age within three years of vaccine introduction in schools.[86] The annual incidence rates of anogenital warts (AGW) in the pre-vaccine periods were 27.8 per 10,000 in female individuals and 26.9 per 10,000 in male individuals. In the postvaccine periods, AGW incidence rates decreased by 31% ($P < 0.001$) in female individuals and 10% ($P = 0.006$) in male individuals; the largest reductions were observed in 15- to 19-year-old female individuals (67%, $P < 0.001$) and male individuals (45%, $P < 0.001$).[85] In a systematic review assessing the effects of HPV vaccine on the incidence of oral and oropharyngeal HPV infection showed a mean relative reduction of 82.7% across different study types and populations.[88] Research shows that the HPV vaccine also induces very high anti-HPV16/18 antibodies that are equivalent for women previously exposed or unexposed to the HPV virus at peak and throughout the plateau phase. These results indicate that prophylactic vaccination is beneficial among women already HPV exposed.[89] Despite the growing evidence highlighting the population-level impact that HPV vaccine on HPV-associated infections, precancers, and cancers, HPV vaccine uptake in the United States has remained considerably below the Healthy People 2030 goal of 80%.[90]

3.4 HPV Vaccine Uptake

Widespread uptake of human papillomavirus (HPV) vaccination could prevent thousands of new infections and mortality due to HPV-caused anogenital warts, cervical, anal, vulvar, vaginal precancers and cancers among men and women**.** HPV vaccine series initiation rates (i.e., receipt of at least one HPV vaccine dose) among 13-17 year olds in the U.S. have gradually increased over the past years, from 60.4% [95% CI: 59.2%-61.6%] in 2016 to 76.9% [95% CI: 75.6%-78.2%] in 2021. HPV

vaccine series completion rates in the U.S. increased from 43.4% [95% CI: 42.1%-44.7%] in 2016 to 61.7% [95% CI: 60.2%-63.2%] in 2021.[92] Despite increases in HPV vaccination rates, uptake levels still falls short of the Healthy People 2030 goal of achieving 80% HPV vaccine series completion rates.[90] In comparison, rates of other adolescent immunizations like the Tdap and meningococcal in the year 2021 were 89.6% [95% CI: 88.6-90.5] and 89.0% [95%CI: 87.9%-90.0%] respectively.[90] Getting a Tdap booster dose is required for school entry for adolescents in all US states.[93] However, most US states, with the exception of Hawaii, Rhode Island, Virginia, and District of Columbia, do not list the HPV vaccine under school entry requirements.[93]

In the US, the federal 'Vaccines for Children' program supplies private and public health providers with federally purchased vaccines for use in children through 18 years of age who are underinsured or uninsured, Medicaid-eligible, or American Indian/Alaska Native.[52] An estimated 32% of adolescents in the US are eligible to receive free vaccines through the VFC program.[52] Most private insurance covers HPV vaccine costs for those in the recommended target and catch-up groups. Despite attempts to mitigate cost as a barrier to promote greater HPV vaccine use, some adolescents are not fully protected against vaccine preventable infections caused by human papillomavirus due to suboptimal vaccine coverage.[92] So far, several studies have examined factors that are associated with low HPV vaccination rates. For example, using the National Immunization Survey- Teen data, researchers have identified growing concerns about the safety of the HPV vaccine, concerns about the adverse events resulting from the administration of the HPV vaccine, not receiving a strong vaccine recommendation from the provider or a 11-12-year well child visit as some of the most commonly cited reasons by parents/caregivers or patients for non-initiation of the HPV vaccine series.[94-98] In fact, in a review of the NIS-Teen data from 2008-2019, the researchers found that the prevalence of self-reported safety concerns or adverse events as the main reason for HPV vaccine refusal increased from 5.3%

[95% CI:4.4%-6.5%] in 2008 to 26.9% % [95% CI:12.0%-13.9%] in 2019.[94] Perceived lack of need or knowledge about the HPV vaccine, younger ages (less than 14 years), not required for school entry, and non-indulgence in sexual activity were also identified as other reasons for refusing/deferring the HPV vaccine.

Researchers have also identified certain racial, sociodemographic as well as socioeconomic factors that influence parental/adolescent's intent to get vaccinated. Rositch and colleagues found that compared with non-Hispanic white parents, parents of minority race/ ethnicity adolescents were more likely to consider the HPV vaccine for their children.[95] Similar findings were reported by Dorell et al., where a significantly higher proportion of parents of girls who were non-Hispanic White, lived in households with higher incomes, and had mothers with higher education levels, delayed and/or refused HPV vaccination.[96] In examining the variations in reasons for non-intention to initiate the HPV vaccine series, Hirth et al. found that Black non-intenders were less likely to report safety, costs, or their children's fear as reasons for not intending to vaccinate their children compared to white non-intenders.[97] Williams et al reported that significantly lower percentage of non-Hispanic Black and Hispanic teens were unvaccinated compared to non-Hispanic white teens in each of the metropolitan statistical area (MSA) categories, i.e., rural, urban, or suburban. However, Black and Hispanic teens were less likely to complete vaccination series after starting it as compared to their white counterparts.[98] Maternal age, maternal education, number of people in the household, and household income were other factors that influenced HPV vaccine uptake among young adolescents.[99-103] For example, mothers with higher education were more likely to cite safety and effectiveness concerns as reasons to defer the HPV vaccine as compared to mothers with a high school education.[101] Similarly, adolescents with a mother aged 35-44 years were less likely to receive the HPV vaccine as compared to adolescents with mothers who were younger than 34 years.[99,100] Also, mothers who were already

seeking cancer prevention services for themselves were more likely to positively influence their daughter's likelihood of getting vaccinated or comply with a law mandating the HPV vaccine.[102,103]

Rural residents face a greater threat of adverse health outcomes due to socioeconomic deprivation, limited access to healthcare, and risk factors for cancer as compared to their urban counterparts.[104] Furthermore, rural communities face a disproportionate burden of health disparities, including low HPV vaccination rates and higher incidence and mortality from HPV-associated cancers.[105] The incidence rate of combined HPV-associated cancer in rural areas between 2009-2003 were slightly elevated (RR = 1.07; 95% CI = 1.06-1.09) as compared to urban areas.[106] Rural females were 11% higher risk for cervical and vaginal cancer and at a 30% higher risk for vulvar cancer as compared to urban women. For oropharyngeal cancers, rural populations had higher rates than their urban peers (RR=1.24, 95% CI: 1.16-1.33). The annual percentage change in the rate of HPV-associated cancers was 90.94% among rural males between 1995 and 2013, compared to a 46.22% increase among urban males.[106]

Disparities in HPV vaccination coverage by metropolitan statistical area (MSA) status were observed in an analysis of 2016 and 2017 National Immunization Survey – Teen (NIS-Teen) data. HPV vaccination initiation among adolescents aged 13-17 years was 11-16 percentage points lower in rural areas and 5-9 percentage points lower in suburban as compared to urban areas signaling that the urban disparity in HPV vaccine uptake has remained consistent over the years.[107] Rural adolescents were less likely to initiate the HPV vaccine series (adjusted odds ratio=0.58, 95% CI: 0.37-0.92) as compared to rural residents after adjusting for demographic, socioeconomic, and healthcare utilization factors but no such difference was observed for vaccine series completion.[108] However, in another analysis of NIS-Teen data, Swiecki-Sikora and colleagues, reported that rural girls (OR=0.74, 95% CI:0.60-0.91) and boys (OR=0.63, 95% CI: 0.41-0.97) had lower odds of completing the HPV vaccine series as compared

to their urban counterparts.[109] Additionally, as noted in a survey of Appalachian women, in rural areas that experiences higher rates of cervical cancer, poverty, limited access to health care, and negative cancer-related attitudes and experiences, fatalistic beliefs like cancer is inevitable and beyond an individual's control may be common, even among young people. These beliefs could function as a barrier for young women from seeking preventive care like HPV vaccination.[110,114] A pilot study assessing parental vaccine knowledge in two Florida counties with extremely low series HPV vaccine completion rates found that a staggering 80% of surveyed parents had little to no knowledge of HPV vaccine.[113]

Several factors influence parental vaccine acceptance in rural areas. For example, in a scoping review, Peterson et al. identified multilevel barriers to and facilitators of HPV vaccine uptake among rural populations. Older age of parent/caregiver, ever having a PAP test or an abnormal PAP test, parental perceptions that their daughters are at risk of cervical cancer, feelings that their daughters are too young to receive the HPV vaccine, and the perception that the vaccine is harmful or painful were identified as barriers to parental acceptance of the HPV vaccine.[111] Being informed about the HPV vaccine and the recommendations, parent/caregiver's awareness of cervical cancer, parental beliefs that the vaccine is beneficial and covered by the insurance, positive parental and peer influences, strong patient-provider relationships, school-based vaccination programs and vaccine reminders, health provider trainings, and social-media marketing campaigns were found to be significant facilitators of vaccine completion.[111]

About 93% of Montana counties are rural and designated as medically underserved but encompass 65% of the state's total population.[112] In 2020, in Montana, the HPV vaccine series completion rate in rural areas (48.6%) was 14.8 percentage points lower when compared to urban regions (63.4%) indicating a significant urban-rural disparity in vaccine uptake.[92] Despite the

introduction of the HPV vaccine and heavy investment in promoting the vaccine, low vaccine uptake and vaccine hesitancy will result in the continued occurrence of HPV-associated cancers in both men and women, particularly in rural areas. Therefore, HPV infection will remain a significant health burden in the upcoming years. The National HPV Vaccination Roundtable Coalition has encouraged researchers to develop and test interventions aimed at increasing HPV vaccine uptake in rural areas as a top priority to tackle the pressing issues of low HPV vaccine knowledge, fatalistic beliefs, and misconceptions about the vaccine among rural parents.[113] Healthcare providers have a crucial frontline role to play in addressing vaccine hesitancy during parent-physician encounters.

3.4.1 Role of providers

Vaccine hesitancy as defined by the World Health Organization's Strategic Advisory Group of Experts on Immunization (SAGE) Working Group are " behaviors that are influenced by a number of factors including confidence (do not trust a vaccine or a provider), complacency (do not perceive a need for the vaccine) and convenience (access) thereby causing a delay in acceptance or outright refusal of vaccination".[121] Vaccine hesitant individuals are a heterogenous group of individuals that may accept all vaccines but remain worried about them, may refuse or delay some but accept other vaccine, or refuse all vaccines.[121] Multiple studies have unequivocally identified providers' strong vaccine recommendation as being most influential in tackling vaccine hesitancy and playing a crucial role parental vaccine decision making process across males, females, and all age groups; yet a lot of providers make these recommendations hesitantly, late, or not at all.[122,123] Provider concerns include the time it takes to recommend the vaccine due to greater parental hesitancy, anticipation of an uncomfortable conversation related to sex and a false perception that parents do not value HPV vaccination.[122] In fact, in a national providers' survey conducted in 2014 almost half of the physicians believed that parents feel HPV vaccine is not or only slightly important for their 11-12-year children[122]

Out of all parent respondents who participated in the National Immunization Survey-Teen (2013-2017), one-third reported not receiving a provider recommendation for vaccination with HPV vaccine for their adolescent.[124] Providers also frequently report facing higher vaccine deferrals or refusals for the HPV vaccine when compared to other adolescent vaccinations.[124] Despite these difficulties, the prevalence of provider recommendations for the HPV vaccine increased from 14.2% in 2011 to 65.5% in 2016.[100]

In a systematic review by Oh et al, provider recommendation was associated with higher likelihood of initiating HPV vaccination (pooled OR= 10.1, CI: 7.6, 13.4) with the odds ratio ranging from 1.1 to 281.2 in analysis of 59 effect sizes. Similarly, provider recommendation was also strongly associated with HPV vaccine series completion (pooled OR=5.2, CI: 1.9, 13.8). Provider recommendation was also associated with higher HPV vaccine series completion after initiation (pooled OR = 1.8, 95% CI: 1.3, 2.5).[120] Based on an analysis of 57 effect sizes, the researchers noted that only 24% of patients initiated the HPV vaccine series without receiving a provider recommendation, whereas an overwhelming 60% of patients initiated the HPV vaccine series after receiving the provider recommendation.[120] Similar findings were reflected in a cross-sectional study evaluating the effects of strong and consistent vaccine recommendations provided by a clinician to their patients on vaccine delivery rates. Higher rates of HPV vaccine series initiation and completion for male [Initiation IRR=1.05, Completion IRR=1.05] and female [Initiation IRR=1.03, Completion IRR:1.04] patients were observed among sites, where clinicians frequently reported always or usually providing strong and consistent recommendations for the HPV vaccine as compared to sites where clinicians, on average reported less frequently strongly recommending the HPV vaccine.[126]

Gold et al. studied the effects of provider discussion topics on HPV vaccine follow through after series initiation. They found that when providers emphasized the need to come back for additional doses with their patients as compared to provider who did not, the patients were 55% more likely to follow through

the recommendations (R= 1.55, 95% CI: 1.18, 2R.03]. However, discussing the benefits of vaccination was not significantly associated with completing the HPV vaccine series (RR=1.06, 95% CI: 0.90-1.25).[127] Gilkey et al. found that a high-quality recommendation was associated with HPV vaccine follow-through (OR = 9.31, 95% CI: 7.10–12.22) compared to no recommendations, but low-quality recommendations did not influence parents' or patients' willingness to come back for additional doses. [128] Fu et al. found that African American children ages 10–12 years were more likely to initiate the HPV vaccine series that visited a provider who "very strongly" recommended the vaccine as compared to those with a provider who "not very strongly" recommended it, therefore underscoring providers' role in increasing HPV vaccine coverage among minority populations.[129]

A high quality recommendation comprised of four essential components, 1) timeliness of the recommendation (routinely recommending the vaccine to 11-12year-olds) 2) consistency-recommending the HPV vaccine to all eligible adolescents 3) adopting the same way, same day approach which is recommending the HPV vaccine along with other adolescent immunizations in the same manner during the clinic visit, and 4) strength-using an univocal language that clearly explains the need and benefits of getting vaccinated.[130] Additionally, using a presumptive approach as a communication strategy while presenting the vaccine and employing motivation interviewing techniques to alleviate parental vaccine concerns are evidence-based approaches to encourage vaccination. A presumptive approach or an announcement approach is where providers initiate their vaccine recommendations using statements that presume parents are ready to vaccinate (e.g., "Your child is due for three vaccines"). This approach to starting a vaccine conversation is different to the participatory approach whereby providers instead engaged parents in dialogue (e.g., "What do you want to about the vaccines today?").[130] Motivational interviewing approaches with regard to immunization encourages providers to inform parents/caregivers about vaccinations according to their specific needs

and their individual level of knowledge, with respectful acceptance of their beliefs. The use of motivational interviewing calls for a respectful and empathetic discussion of vaccination and helps to build a strong provider-patient relationships.[131]

In a survey of 2422 parents of 9-to-17-year-old children, researchers found that receiving strong vaccine recommendations not only motivated parents to consider vaccinating their children, but also increased the odds of agreeing that the HPV vaccine is safe by 7 times and the odds of agreeing they were not concerned about side effects by 2 times compared to parents who had not received a strong recommendation.[132] Dempsey et al. conducted a randomized controlled trial to assess how a provider communication intervention aimed at improving HPV vaccination uptake influences parental vaccine beliefs. Providers in the intervention arm received were given promotional materials and were trained in 'presumptive recommendations' and 'motivational interviewing' vaccine communication strategies to provide very strong recommendations. Receipt of a 'very strong' vaccine recommendation was associated with greater perceived urgency to get vaccinated, greater trust in the information received form the provider, decreased vaccine hesitancy, increase vaccine recipient.[133] Brewer and colleagues developed and deployed a brief announcement approach-based training for providers to use a presumptive announcements, address parental vaccine hesitancy, and raise topic of HPV vaccination at a later visit if parents refused in 29 clinics. Clinics that received the announcement approach-based training had increases in HPV vaccine initiation rates among 11- to 12-year-old children that were 5.4 percentage points higher than control clinics, whereas clinics receiving conversation training showed no difference from control clinics.[134] Also, the Announcement Approach-based training was associated with increases in positive attitudes toward HPV vaccine, improved social norms, higher self-efficacy to recommend the vaccine, and higher intentions to do so among participating providers.[139] Findings from another qualitative study by Niccolai et al found that parents were less "enthusiastic" about getting their

children vaccinated if the providers presented the vaccine as “optional” or “ recommended” instead of required as it propagated to a perception that the vaccine is low priority.[135] Health providers play an important role in disseminating information and establishing norms surrounding HPV vaccine [136]

3.5 Conclusion

Because of relatively low rates of HPV vaccination in Montana, the importance of providers’ vaccine recommendations and understanding health care personnel’s knowledge, attitudes, and professional practices regarding the HPV vaccine are crucial for developing evidence-based interventions focused on improving the consistency and strength of vaccine recommendations.[136] Provider recommendation would help to facilitate an improvement in vaccine acceptance and vaccination intentions. Studies in the past have shown that clinician and healthcare system-based interventions have a greater impact on improving HPV vaccination rates among adolescents when compared to efforts primarily focused on parental beliefs or knowledge.[137] There is a relative shortage of pediatricians in rural areas and multiple studies on provider vaccine recommendations have also noted that as compared clinicians in pediatric practice, family medicine practitioners were half as likely to provide strong and consistent recommendations for the HPV vaccine.[126] Tapping into the potential of the existing healthcare workforce that is endowed with the skills to influence health behaviors and harnessing their expertise in HPV vaccine promotion can be crucial. Other health care workers (e.g., nurses and medical assistants) are well-positioned to discuss HPV vaccination with parents and adolescents. These health professionals are endowed with ample opportunities to build stronger rapport and trust with patients and their parents before recommending HPV vaccine.[139] Additionally, nurses and medical assistants serve important roles in recommending vaccination in non-traditional settings, such as school health centers and school-located mass vaccination camps, public health departments,

rural health centers, etc. or could be the only health professionals that parents interact with during a clinic visit.

In previous research conducted in Montana, physicians, and public health stakeholders identified greater parental/patient informational needs and limited time for vaccine discussions as barriers to HPV vaccination, potentially leading to missed opportunities.[138] Non-physician providers, like nurses, could help bridge this gap and serve as champions and promoters of the HPV vaccine. Nurses play a significant role in vaccine delivery services by educating parents and patients on vaccines, alleviating parental concerns about vaccines, and promoting greater community health goals. Even though nurses serve as primary stakeholders in developing and implementing HPV vaccine promotion activities in their clinic practices, there is limited published data focused on understanding their knowledge, attitudes, and beliefs about HPV-related disorders and the HPV vaccine.

Chapter 4: Specific Aims

4.1 Specific aims and methods

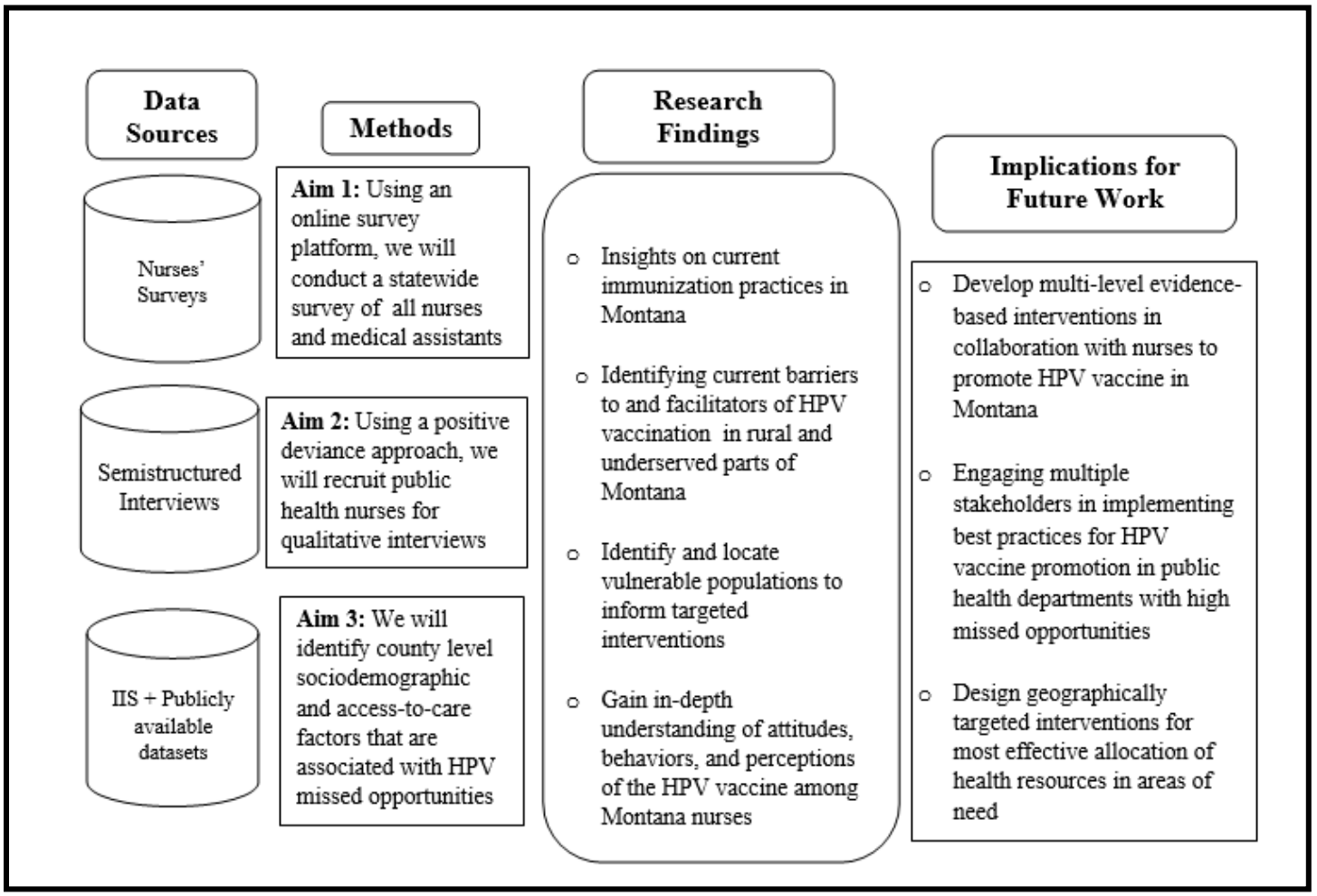
<u>Aim 1</u>: To determine the role of nurses and medical assistants in improving HPV vaccination rates in Montana. Nurses play a significant role in vaccine delivery services by educating parents and patients on vaccines, alleviating parental concerns about vaccines, and promoting greater community health goals.[1] Even though nurses serve as primary stakeholders in developing and implementing HPV vaccine promotion activities in their clinic practices, there is limited published data focused on understanding their knowledge, attitudes, and beliefs about HPV-related disorders and the HPV vaccine.[2-4] Thus, designing interventions to ensure healthcare professionals other than pediatricians are familiar and confident with adolescent vaccine recommendations is extremely important in large, rural states like Montana.[5] For this research aim, we conducted a statewide survey of Montana nurses and medical assistants working at facilities participating in Vaccine for Children program, as their perceptions and experiences regarding current barriers to HPV vaccine uptake are critical to informing strategies to improve HPV vaccination rates.

<u>Aim 2:</u> To identify nurse- and clinic-level facilitators of HPV vaccination in rural public health departments in Montana: Missed opportunities are clinical encounters when an age-eligible adolescent receives one or more recommended vaccination but does not receive the HPV vaccine.[5] Rural populations have been underrepresented in prior research on strategies to increase HPV vaccine uptake. Research focused on increasing vaccination rates in rural populations is needed to decrease the incidence of HPV-associated cancers. Adolescents residing in rural areas are more likely to use non-traditional facilities like public health clinics for their immunization needs when compared to those residing in suburban and urban areas.[5] In these public health facilities, public health nurses regularly

interact with children and adolescent patients and their parents/guardians.[6] For this research aim, using a positive deviance framework,[7] we recruited nurses working at rural public health departments with both high and low missed opportunity rates for HPV vaccination to determine patient-, provider-, and clinic-level factors associated with high or low HPV vaccine uptake. The findings from this study will inform development and deployment of evidence-based best practices to increase HPV vaccine coverage in rural areas.

<u>Aim 3:</u> Identify county-level socio-demographic and access-to-care factors associated with missed opportunities for HPV vaccination in Montana: In October 2018, the President's Cancer Panel cited reducing missed clinical opportunities to recommend and administer the HPV vaccine as a top strategy for increasing HPV vaccination coverage in the country.[8] In 2021, the HPV series initiation rate in Montana was 76.9%. In comparison 89.6% of adolescents had received tetanus-diphtheria-acellular pertussis (Tdap) vaccine, signaling missed opportunities.[9] Quantification of missed opportunities in Montana by counties revealed high variability in the rates ranging from 31.1% to 92.3%; with rural counties reporting higher missed opportunities as compared to urban areas. In the same report, public health departments had significantly greater missed opportunities (64.9%) as compared to private (49.7%) and Indian/Tribal Health Services (37.7%).[6] An in-depth understanding of county-level socio-demographic and access to care factors associated with these missed opportunities is warranted for optimum allocation of limited health resources and to inform geographically targeted interventions. Using a population-based secondary analysis of Montana's immunization information system data, we determined county-level sociodemographic and access-to-care correlates of missed opportunities to inform geographically targeted interventions. Data for sociodemographic and access-to-care factors were extracted from publicly available datasets.[10-13]

Figure 4.1 Dissertation project overview with study methods



The *long-term goal* of this project is to optimize the impact of nurses and medical assistants in HPV vaccine promotion in rural states like Montana. The *objective* of this project was to collate state-level data on the knowledge, attitudes, beliefs, perceptions, and current practices of nurses and medical assistants regarding the HPV vaccine and to identify county-level sociodemographic and access to care factors associated with missed opportunities for HPV vaccination. The *central hypothesis* is that by engaging nursing staff in HPV vaccine promotion, we will be able to improve the vaccination rates in Montana and achieve the Healthy People 2030 goal. The underlying *rationale* is that vaccinating adolescents with the HPV vaccine will have critical public health and economic implications.

4.2 Innovation of the proposed project

For this project, our objectives were designed to tackle research gaps in best practices for HPV vaccination uptake that are identified as top priorities by the National HPV Roundtable Coalition.[14] Through this project, we will be able to generate knowledge that is foundational in developing novel approaches aimed at improving HPV vaccine uptake for rural and medically underserved areas, which could also be emulated by other US states with similar geographic and socio-demographic structures. The project findings will facilitate designing multi-level interventions to improve HPV vaccination rates in Montana.

4.3 References

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Chapter 5: Nurses' perceptions, experiences, and practices regarding human papillomavirus vaccination: results from a cross-sectional survey in Montana

5.1 Abstract

Background: Nationally, much of the focus on improving human papillomavirus (HPV) vaccine uptake has been on effective strategies physicians can use to promote vaccination. However, in large, predominately rural states like Montana, nurses and medical assistants play critical roles in immunization services delivery, and their viewpoints are imperative in designing strategies to increase vaccination rates.

Methods: We designed, pilot-tested, and disseminated an online survey instrument to nurses and medical assistants working in clinics participating in the Vaccines for Children program in Montana. Survey questions focused on clinic vaccination practices, respondents' perceptions of the HPV vaccine, perceived barriers to vaccine uptake, and general opinions on potential strategies to improve HPV vaccination rates.

Results: We analyzed data from 227 respondents. Overall, 90% of nurses strongly agreed or agreed that the HPV vaccine is important and had confidence in the vaccine's safety. More nurses reported experiencing greater parental vaccine refusal or delay for male patients regardless of age. About 53.7% of nurses reported that their clinics had reminder/recall systems to encourage parents to bring their children for vaccination. Nurses identified misinformation from social media, infrequent wellness visits, and vaccine safety concerns as barriers to HPV vaccine uptake.

Conclusion: Study findings identified several promising initiatives to accelerate vaccination in primarily rural states like Montana, including promoting widespread adoption of reminder/recall systems, training nurses in evidence-based techniques to provide strong vaccine recommendations, and

leveraging social media to disseminate consistent messages about the HPV vaccine recommendations for both sexes and its role in cancer prevention.

5.2 Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States, with 13 million new cases emerging every year.[1] Although most HPV infections are asymptomatic and are self-limiting, persistent HPV infection can cause cervical cancer in women as well as other anogenital cancers, oropharyngeal cancer, and genital warts in men and women.[2,3] The U.S. Advisory Committee on Immunization Practices (ACIP) routinely recommends HPV vaccination at the age of 11 or 12 years; however, vaccination can be given starting at the age of 9 years.[4] If the first vaccine dose is received before the 15th birthday, then two vaccine doses are required to complete the series; otherwise, three doses are needed for series completion.[5] Since it was first licensed in 2006, HPV vaccination has been instrumental in significantly reducing HPV-related infections, precancers, and cancers. In a recent observational study from the United Kingdom, the researchers found an 87% (95% CI 72-94) reduction in cervical cancer rates and a 97% (95% CI 96-98) reduction in grade 3 cervical intraepithelial neoplasia (CIN3) in women who completed their HPV vaccine series between 12-13 years as compared to an unvaccinated cohort.[6] Additionally, multiple studies analyzing surveillance data on the HPV vaccine have supported the safety of the vaccination in adolescents.[7,8,9] Despite its proven safety and effectiveness, HPV vaccine uptake has remained consistently low over the years at the national level in the U.S.[10,11]

Rural communities in the U.S. face a disproportionate burden of health disparities resulting from a complex interplay between a host of factors like barriers to accessing primary care services; higher rates of un- or under-insurance; lower health literacy, and vaccination rates; and a shortage of pediatricians.[12,13,14,15] Indeed, pediatricians contribute to higher vaccine uptake in their communities.

For example, pediatricians more often administered HPV series to their patients and reported higher confidence in their ability to address HPV vaccine concerns when compared to family care practitioners.[18,19,20] Rural areas have also been associated with negative parental attitudes about the HPV vaccine, and higher incidence and mortality from HPV-caused cancers.[16,17] In Montana, a large and primarily rural state, the HPV vaccine series completion rate in 2020 was 54.4% for adolescents ages 13-17 years, as reported by the Centers for Disease Control and Prevention's National Immunization Survey-Teen, far below the Healthy People 2030 goal of 80%.[21,22] Furthermore, for the years 2015-2019, the proportion of rural adolescents in Montana who received at least one dose of the HPV vaccine (56.0%) was 11.9 percentage points lower when compared to Montana adolescents living in more urban areas (67.9%), indicating a pronounced urban-rural disparity in vaccine uptake.[22] Despite having a vaccine that prevents cancer, high levels of protection against HPV-associated infections at individual and population levels remain inadequate due to lower uptake.

In a research study by Newcomer et al., physicians and public health stakeholders in Montana identified greater parental/patient informational needs and limited time for vaccine discussions as barriers to HPV vaccination.[23] Non-physician healthcare providers, like nurses, could help bridge this gap and serve as champions and promoters of the HPV vaccine. Adolescents residing in rural areas are more likely to use non-traditional facilities like public health clinics for their immunization needs when compared to those residing in suburban and urban areas.[12] In public health facilities, nurses and medical assistants regularly interact with children and adolescent patients and their parents/guardians. Past studies have consistently shown that absent or weak recommendations from healthcare providers drive poor vaccine uptake[24,25] Thus, designing interventions to ensure that healthcare professionals other than pediatricians are familiar and confident with adolescent vaccine recommendations is crucial in predominately rural states like Montana with higher health professional shortage areas. Nurses play a

significant role in vaccine delivery services by educating parents and patients on vaccines, alleviating parental concerns and vaccine hesitancy, promoting greater community health goals, and are well-positioned to facilitate coordination efforts within their practices.[26,27,28] Although nurses serve as primary stakeholders in developing and implementing health promotion initiatives in their practices, there are limited published data focused on understanding nurses' perspectives on HPV vaccination.[29,30,31]

To address this research gap, we designed a cross-sectional study to determine Montana nurses' and medical assistants' perceptions, experiences, and practices in providing adolescent immunization services, with a focus on HPV vaccination. Through our study findings, we identified recommendations that can inform initiatives to effectively engage nurses in improving HPV vaccination rates in states with high rural and medically underserved populations.

5.3 Methods

4.3.1 Survey Population: The sample population for this study consisted of registered nurses (RNs), advanced practice registered nurses (APRNs), and medical assistants in Montana currently employed at a facility that participated in the federal Vaccine for Children (VFC) program. The VFC program provides childhood and adolescent vaccines to enrolled providers for immunizing eligible children through 18 years of age at no cost.[32] Since its implementation in 1994, the Centers for Disease Control and Prevention (CDC) has estimated that the VFC program has been instrumental in saving about 295 billion dollars in direct costs by 2013.[57] Over 90% of facilities that provide immunization services to children in Montana participate in VFC.

4.3.2 Survey Design and Testing: An online survey instrument was developed and administered using the electronic database REDCap, hosted by the University of Washington Institute of Translational Health Sciences.[33] The survey questionnaire was developed based on a review of existing literature on

vaccine attitudes and previous CDC-funded surveys of primary care physicians' perspectives on HPV vaccinations.[18,19,20] The final survey tool comprised five sections. The first section collected information on the participants and their medical roles and responsibilities. We designed the second section to learn more about clinic vaccination practices, including the use of reminder/recall systems. Reminders alert patients about vaccinations that will be due in the future and recall messages are used to inform patients about the vaccinations that are overdue.[34,35] In the third section, we included questions on nurses' perceptions regarding the HPV vaccine, their experiences with parental awareness and refusal or deferral of the HPV vaccine, and perceived barriers to adolescents receiving the HPV vaccine. Section four had questions on the nurses' vaccine attitudes, beliefs, and perceptions of the effectiveness of strategies for improving the HPV vaccination rates; and the last section contained a few demographic questions. (Appendix A) Participants could utilize comment boxes throughout the survey to provide additional open-ended feedback.

The survey instrument was pre-tested and modified based on cognitive interviews with a convenience sample of six nurses and one medical assistant. Survey pre-testing was conducted on a virtual platform. We used cognitive interviewing techniques (Think-aloud approach and Verbal probing) to walk nurses through the survey and collect their feedback on the comprehensibility of the questions and overall survey design.[36] Most comments were positive, with participants emphasizing the need for a state-wide survey on this topic. Based on pre-testing, we estimated that most participants would be able to complete the survey within 12-15 minutes. Nurses and medical assistants who participated in the pre-testing were given a $20 gift certificate for their time and input and were not excluded from participating in the survey. The final survey instrument had a total of 23 content questions and 6 demographic questions.

4.3.3 Survey Implementation: We obtained a list containing the email addresses of VFC coordinators from the Montana Department of Health and Human Services Immunization Program section. We sent an email containing a short study description, the study team's contact information, and the survey link to these contacts in November 2020. The VFC coordinators were requested to distribute the survey among all nurses and medical assistants working in immunization services in their facilities. VFC coordinators who were practicing nurses and provided immunization services to adolescents were encouraged to take the survey as well. We sent two additional email reminders to the VFC coordinators after the initial survey invitation at equal intervals of 30 days, after which the survey was closed in early March 2021. After the study closure, three participating nurses were randomly selected to receive a $30 gift card. We received approval from the University of Montana Institutional Review Board to conduct this study.

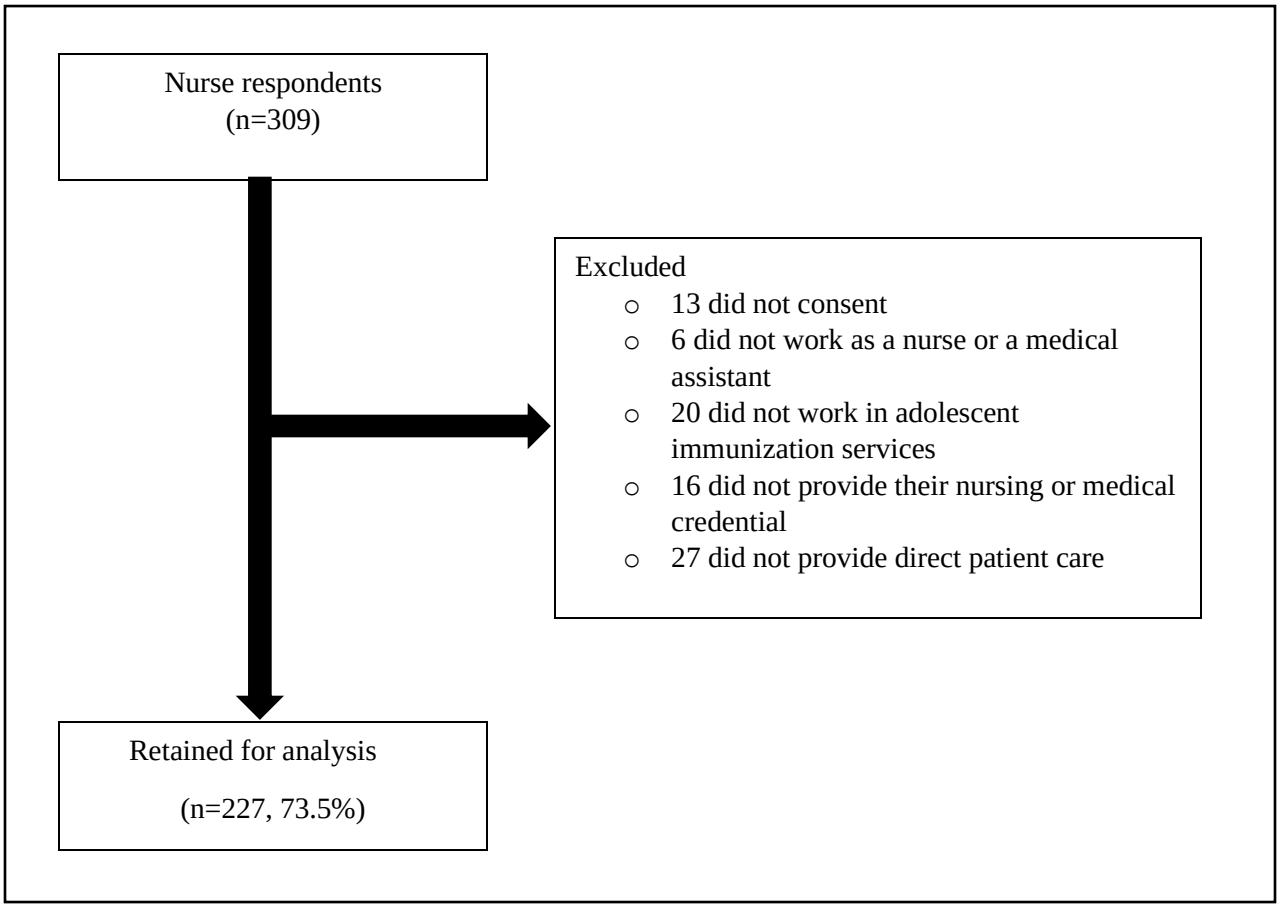
4.3.4 Power Analysis: Among study respondents, 61 nurses reported working in a public health facility, and 201 nurses reported working in other healthcare facilities (private hospitals and other facilities). Assuming that 70% of nurses working in a public health facility reported having high confidence in the safety of the HPV vaccine, we will have 80% power to detect a 20-percentage point difference in the proportion of nurses working in a private/another facility also reporting having high confidence in the safety of the HPV vaccine (alpha=0.05).

5.4 Results

We received a total of 309 responses, and 296 nurses provided their consent to participate in the survey. Of these 296 nurses, n=6 reported that they did not currently work as either a nurse or medical assistants in the state of Montana and n=20 reported that they were not involved with adolescent immunization services; these respondents were excluded. Out of the remaining 270 respondents, we further excluded n=16 respondents who did not provide their nursing or medical credential and n=27

who reported not currently working in direct patient care. Our final analytic sample consisted of 227 respondents. (Figure 5.1)**.** All statistical analyses were performed using SAS version 9.4 (SAS Institute, Inc, Cary, NC)

Figure 5.1: Flow diagram detailing survey eligibility



Characteristics of respondents: Of the 227 eligible respondents, most (55.9%) were registered nurses or advanced practice registered nurses, 26.0% were medical assistants, and 17.6% were licensed practical nurses. A majority (94.2%) of the respondents were female and identified themselves as being white (77.1%). About 4.0% of the respondents identified themselves as American Indian or Alaska Native. About 27.4% of the respondents belonged to the age group of 41-50 years, followed by 23.2% of the respondents who reported being in the age group 51-60 years. Approximately 33.0% of the

participants reported working as a nurse or a medical assistant for more than 20 years, 18.2% for about two to six years, and 17.0% for around six to ten years. Only 7.0% of the nurses in our analytic sample had less than two years of experience working as nursing professionals. (Table 5.1)

Practice Characteristics: While 36.1% of respondents either worked in an independent private clinic or a hospital-based clinic, 19.4% worked at a public health department, and the rest of the respondents (39.7 %) either worked at a community health center, a rural health clinic, a school-based clinic, or a different type of immunization clinic. About 5.0% of respondents did not report their clinic setting. About half of the respondents examined five or fewer 9-17-year-old patients in a typical week. While all respondents were involved in providing immunization services to adolescents, over 85.0% of respondents reported recommending vaccines to adolescents and their parents or caregivers and interacting with them to answer vaccine-related questions. About two-thirds of the respondents reported scheduling clinic visits for immunizations, and about 60.0% reported overseeing vaccine ordering and managing vaccine inventory at their clinics. About 50.0% of the respondents reported that over half of the patients visiting their facility were eligible to receive free vaccines under the VFC program. (Table 5.1)

Table 5.1: Respondent and Practice Characteristics

	n *(N=227)*	%
Nursing Credentials		
Registered Nurse (RN/APRN)	127	55.9%
Licensed Practical Nurse (LPN)	40	17.6%
Medical Assistant or Other	60	26.4%
Age, in years		
21-30 years	36	15.9%
31-40 years	41	18.1%
41-50 years	52	22.9%
51-60 years	44	19.4%

≥61 years	16	7.1%
Prefer not to answer or Missing	38	16.7%
Sex		
Male	9	4.0%
Female	180	79.3%
Prefer not to answer or Missing	38	16.7%
Clinic Setting		
Public health department-operated clinic	44	19.4%
Private practice or a hospital/university-based clinic	82	36.1%
Other*	90	39.7%
Missing	11	4.9%
Practice Location		
Non-Metropolitan Statistical Area	85	37.4%
Micropolitan Statistical Area	58	25.6%
Metropolitan Statistical Area	47	20.7%
Missing	37	16.3%
Estimated number of 9-17-year-old patients seen in a typical week		
≤5 patients	118	52.0%
6-20 patients	74	32.6%
>20 patients	23	10.1%
Not Sure	12	5.3%
Estimated percentage of 9-17-year-old patients eligible to receive vaccines under the VFC program**		
<25%	24	10.6%
25%-49%	58	25.6%
50%-75%	68	30.0%
>75%	35	15.4%
Not Sure	27	12.0%
Missing	15	6.6%

Column percentages do not always total to 100% due to rounding of the values, * includes a community health center, rural health clinic, migrant health center, Indian Health Service (IHS)-operated center, Tribal health facility, or urban Indian health care facility, Military health care facility (Army, Navy, Air Force, Marines, Coast Guard), WIC clinic, school-based clinic, and any other clinic type, ** VFC indicates Vaccine for Children federal program

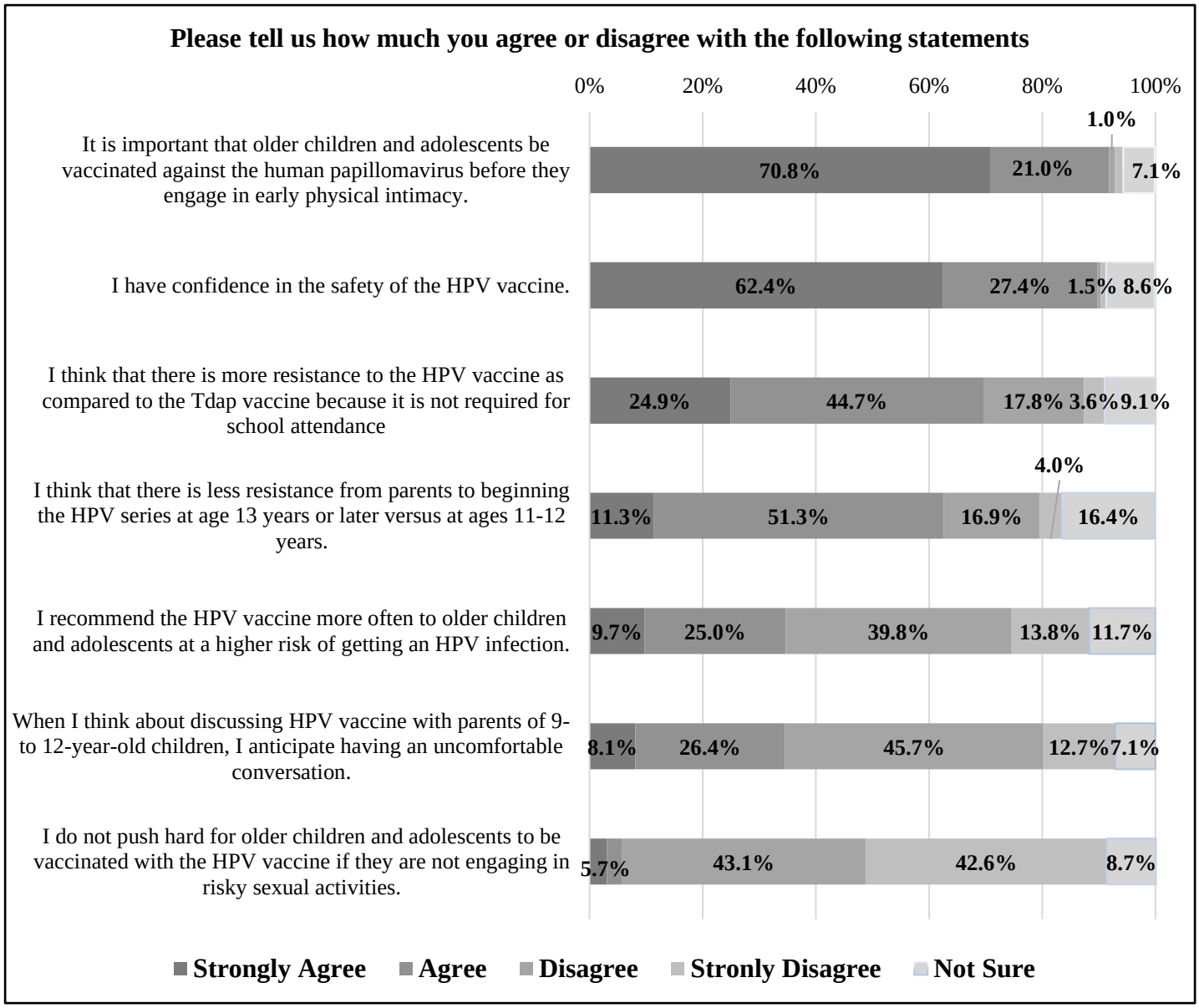
Use of Reminder/Recall (R/R) Systems for HPV Vaccination Delivery: About 52.0% of respondents reported using some form of reminder/recall (R/R) processes at their clinics to identify and contact parents/caregivers of adolescents who are due or overdue to receive recommended immunizations. Of those that use some form of R/R at their facilities, about 28.9% of respondents reported that staff availability dictated how often they were able to generate them, and about 25.0% of the nurses responded being able to generate the R/R lists monthly. The most common mode of R/R delivery was by phone (38%), a paper letter or a postcard (30.8%), or a text message (10.1%).

Specific to R/R processes for completing the multi-dose HPV vaccine series, most respondents reported that parents were told when they needed to return for the second dose at the initial vaccine appointment (63.4%) or that the subsequent immunization visit was scheduled during the initial appointment (55.5%). Only 26.9% of respondents reported that their clinics proactively reached out to parents or patients to remind them to return for additional HPV vaccine doses, and 5.3% of nurses reported that their clinics had no process to remind adolescents and their caregivers to return to complete the HPV vaccine series.

Attitudes, Beliefs, and Experiences with HPV Vaccination Delivery: About 90.0% of nurses agreed or strongly agreed that it was important that older children and adolescents be vaccinated against HPV before they engage in early physical intimacy, and a similar percentage (89.8%) expressed confidence in the safety of the HPV vaccine. However, about 34.5% of respondents reported anticipating an uncomfortable conversation while discussing the HPV vaccine with parents of 9 to 12-year-old children. Over two-thirds of respondents (69.6%) reported facing more resistance to the HPV vaccination as compared to the tetanus-diphtheria-acellular pertussis (Tdap) vaccine since Tdap vaccination is required by Montana state law for school attendance.[13] About 62.6% of nurses reported that parents prefer to initiate the HPV vaccine series for their children at 13 years or older versus at

younger ages. Approximately one-third of nurses reported recommending the HPV vaccine more often to age-eligible adolescents at a higher risk of getting an HPV infection. (Figure 5.2).

Figure 5.2: Nurses' attitudes, beliefs, and experiences regarding human papillomavirus (HPV) vaccination for older children and adolescents

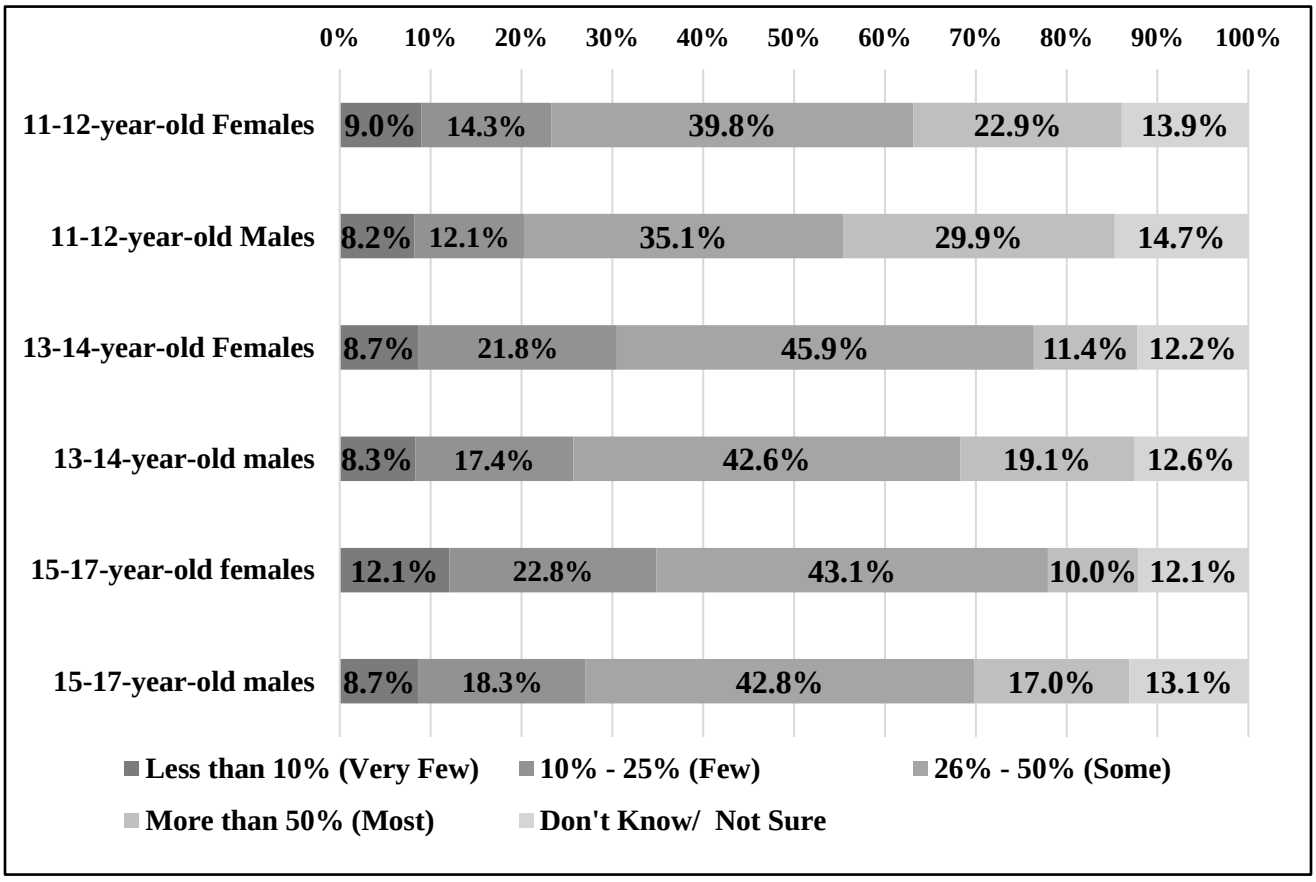


Perceived Barriers to HPV Vaccine Delivery: More than two-thirds of nurses reported that they perceived the following as significant barriers to recommending and administering the HPV vaccine: parents not thinking that the vaccine is necessary for their sons (74.5%), misinformation that parents

receive from the internet or social media (71.6%), parental concerns about the safety of the HPV vaccine (67.7%), and irregular well-child visits (66.7%). Over half of respondents felt that the amount of time it takes to discuss HPV vaccination with parents or adolescents or the financial cost to get the HPV vaccine were not at all barriers to recommending or administering the HPV vaccine. Through open-ended text box responses, nurses reported additional barriers to the HPV vaccination with the most frequently reported barriers being patient concerns about injection site pain, effects of the COVID-19 pandemic on regular well-child visits, and parental consent to receive the HPV vaccine. Respondents reported that parents of younger children (11-12-year-olds) were less aware that HPV vaccination is recommended for their child as compared to parents of older children (15-17-year-olds).

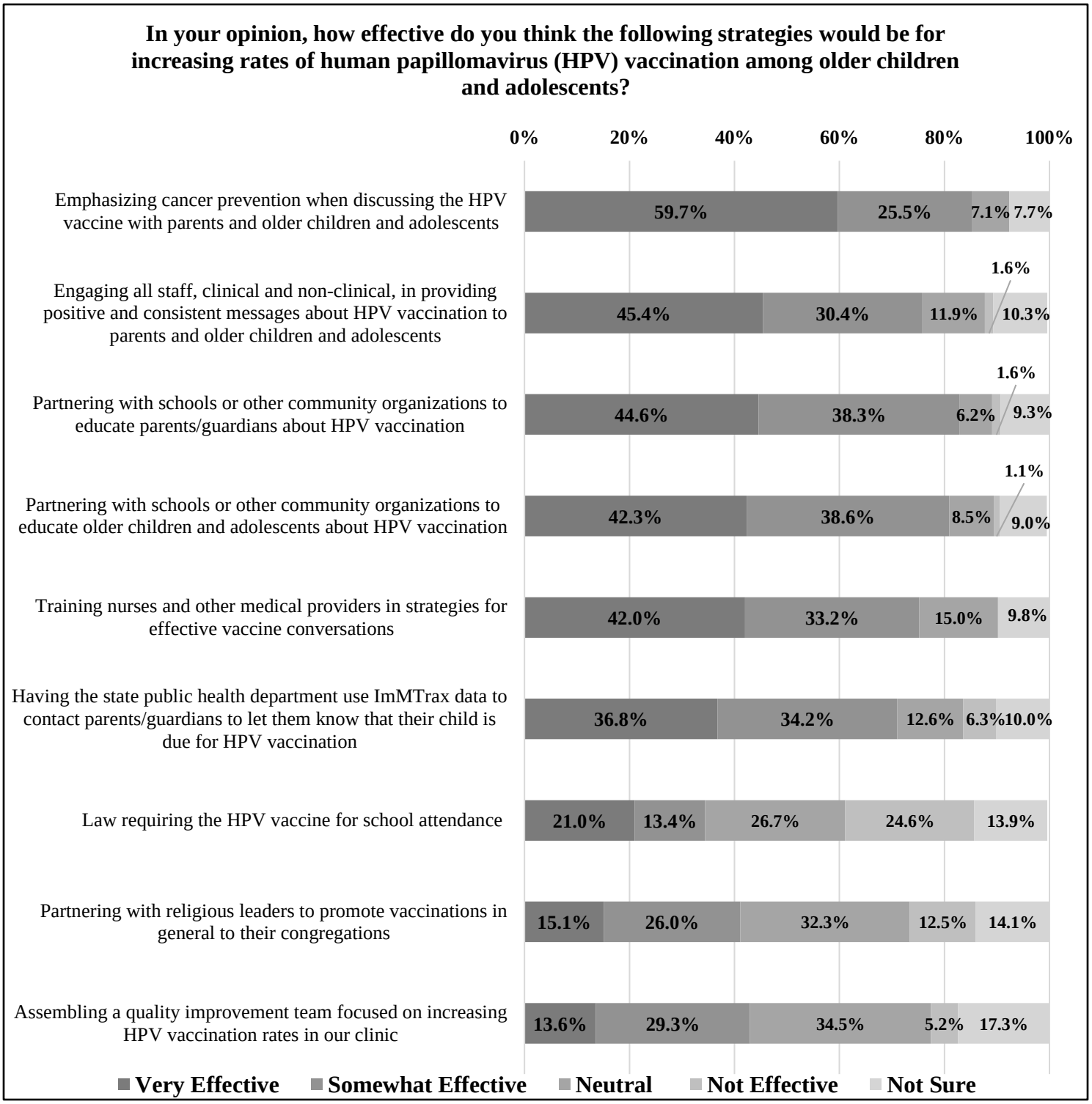
A higher proportion of respondents reported over half of parental refusal or deferral of the HPV vaccine among younger age groups (11-12-year-olds) compared to older adults (15-17-year-olds) regardless of the adolescent's gender. (Figure 5.3).

FIGURE 5.3: Nurses' report of the estimated percentage of parents who defer HPV vaccination, by age group and adolescent's gender



Nurses' Support of Strategies to Improve HPV Vaccination Rates: Interventions and initiatives that were strongly supported by over three-fourths of the nurse respondents were emphasizing cancer prevention when discussing the HPV vaccine with parents and adolescents (85.5%), partnering with a school or other community organizations in educating adolescents and parents about HPV vaccination (82.0%), engaging all staff, clinical and non-clinical, in providing positive and consistent messages about HPV vaccination (75.8%), training nurses and medical providers in strategies for effective vaccine conversations (75.2%). Implementing a state law requiring the HPV vaccine for school attendance was least supported by the respondents (34.4%) as a strategy to increase vaccine uptake. (Figure 4) In open-ended responses, nurses provided additional ideas regarding initiatives to increase HPV vaccination including school-based vaccination clinics, incorporating immunizations within sports physicals, and providing education about the HPV vaccination through T.V. commercials or mailers.

Figure 5.4: Nurses' support of strategies to improve HPV vaccination rates



5.5 Discussion

Despite substantial evidence on the safety and efficacy of HPV vaccination in preventing oropharyngeal and anogenital cancers, vaccine uptake is lower than established public health goals in Montana, particularly among rural adolescents. Prior research has highlighted the influential role that primary care providers, typically pediatricians and family medicine practitioners, play in promoting HPV vaccination.[37,38] However, there has been less work focused on the important role of nurses in adolescent immunization services delivery efforts. Our study attempted to fill this significant gap in research related to nurses' perceptions, experiences, and practices regarding HPV vaccination among older children and adolescents. Results from this study indicate that HPV vaccination was widely supported by Montana nurses, who also expressed confidence in the safety of the vaccine. Nurse respondents identified various barriers to HPV vaccine uptake in their communities, including parents' lack of knowledge regarding which vaccines are recommended for adolescents, misinformation from social media, and specific parental concerns about the HPV vaccine. Importantly, nurses offered their input on strategies to increase vaccination uptake. Overall, the results from this survey point to several avenues for effectively engaging with nurses and medical assistants in HPV vaccination promotion efforts.

A provider's strong recommendation is one of the most influential factors in parental decisions to get their children vaccinated against HPV.[24] However, about one-third of the survey respondents reported anticipating an uncomfortable conversation while discussing the HPV vaccine with adolescents or their parents. In our study findings, nurses indicated receptiveness toward training in effective vaccine conversations. Nationally, multiple studies on providers' vaccine communication styles are linked with increased child and adolescent vaccine uptake, with a presumptive approach (i.e., assuming the parent intends to vaccinate) being more effective than a participatory style (i.e., asking if

the parent would like to consider vaccination).[39,40,41,42] There is also increasing attention toward motivational interviewing (MI) strategies that can be used to counsel vaccine-hesitant parents and address parents' specific vaccine concerns. Motivational interviewing uses a collaborative conversation style to propel positive health behavior change and strengthen an individual's motivation to change. [43,44] The four motivational interviewing elements of open-ended questions, affirmations, reflection, and summary are built on the core principles of nursing practice which are connecting with the patient, evoking trust, and empathic listening.[45] A Swedish study focused on evaluating the proficiency of nurses in conducting motivational interviews with their patients indicated a need for nurses to receive additional training, feedback, and supervision in clinical practice with motivational interviewing techniques to achieve proficiency.[46] Empowering nurses to deliver strong vaccine recommendations and use MI techniques with vaccine-hesitant parents and caregivers may enable them to play a stronger role in increasing vaccination confidence and HPV vaccination uptake in their communities.[45]

Reminder/recall systems are evidence-based practices that have been shown to increase vaccination rates among children, adolescents, and adults.[35,47]. The Task Force on Community Preventive Services recommends clinics perform some form of reminder-recall for their patients to improve vaccination rates.[47] In a narrative review about the contribution of reminder-recall systems to vaccine delivery efforts, Kempe et. al reported a 29% increase in adolescent vaccination rates at facilities that utilize reminder/recall processes.[35] In our study, nurses reported inconsistent use of reminder-recall systems for prompting parents to bring their children in when vaccines are due or past due. Previous studies analyzing providers' perspectives have cited limited staff time, competing demands, insufficient technology, and increased costs as barriers to the successful implementation and sustenance of R/R systems.[48,49] Providers in Montana, in which 90% of the counties are designated as health professional shortage areas [50], face similar challenges in their primary care practices which limit

their ability to implement R/R processes. Innovative approaches such as centralized R/R systems may address the feasibility challenges of practice-based R/R in rural and medically underserved areas. Centralized R/R is conducted centrally either through healthcare systems or public health departments using an immunization information system.[35] Although large-scale implementation research studies evaluating the effects of centralized R/R systems on HPV vaccination rates only showed modest increases, these improvements could have a significant impact on reducing HPV-associated infections on a larger population level in the long run.[51,52] Centralized R/R may be instrumental in reducing the burden on nursing professionals and awarding them more time to engage with parents and patients at their clinics.

Finally, the results from our survey indicate a need to increase community awareness of the HPV vaccine and the dosing schedule. Approximately 60% and 67.7% of survey respondents estimated that fewer than half of parents of 11-12-year-old females and males respectively were aware that the HPV vaccine was recommended for their children. Additionally, nurses also reported that parents' refusal or deferral of the HPV vaccine was more common with 11-12-year-old children than with children ages 13 or older. Early marketing campaigns for the HPV vaccine were geared towards the prevention of sexually transmitted infections which caused discomfort among parents and providers while discussing the vaccine. Even though there has been a push to emphasize cancer prevention instead, safety concerns from parents and the public are still prevalent, owing to which parents have higher informational needs regarding the HPV vaccine relative to other vaccines.[23] Parents' need for enhanced information and discussion may be a barrier to 11- or 12-year-old children getting the vaccine as recommended if this is the age when a trusted health professional first brings up the vaccine. Therefore, to increase on-time HPV vaccine uptake at ages 11-12 years, there is a need for widespread education of parents about recommended adolescent vaccines at earlier ages. National organizations like the American Cancer Society and the American Academy of Pediatrics have updated their recommendations to encourage

providers to initiate the HPV vaccine series as early as 9 years of age.[53,54] Starting the HPV vaccine series earlier at 9 years will likely lead to greater parental engagement and higher on-time vaccination rates. Providers will have the advantage of disengaging from framing the vaccination as a means of preventing a sexually transmitted infection and instead emphasizing cancer prevention while promoting the vaccine to their patients or parents. Furthermore, earlier vaccine series initiation provides more of an opportunity to complete the series before the adolescent is due to receive school-entry required or other age-appropriate vaccines.[53] In this survey, many nurses reported being in favor of partnerships with schools or other community organizations to educate families about the HPV vaccine. Building community collaborations to leverage the reach of opinion leaders in spreading positive messages about the HPV vaccination can help increase vaccine uptake.[55]

Our study findings align with findings from a qualitative study of healthcare personnel in rural Kentucky in suggesting that nursing professionals have a prominent role in assisting parents as they navigate health-related decisions for their children.[56] Future studies are needed to develop and test communication strategies for nurses to effectively counsel and encourage parents and adolescents to receive the HPV vaccine. Nurses play a pivotal role in the ongoing efforts to increase awareness about the importance, safety, and effectiveness of the HPV vaccine.[27] As healthcare professionals who are readily accessible to families and adolescents, nurses are well-positioned to positively influence health behaviors and bring change to their communities.[31]

Our study had some limitations. We did not administer the survey to a fixed number of nurses and medical assistants. So, we were not able to compare the characteristics of respondents and non-respondents or produce a response rate. However, the metropolitan statistical area status-related distribution of 63.0% of rural nurses and 20.7% of urban nurses is representative of the geographic distribution of nursing professionals in Montana. Since this was a self-administered survey, the

responses could be subjected to social desirability and recall bias. However, the anonymous nature of our survey may have reduced that likelihood. Finally, because our survey population consisted of nurses from Montana, the generalizability of the findings to nurses in other regions may be limited. However, given the urgent need to address persistently low HPV vaccination rates in rural areas of the U.S., this study of nurses and medical assistants in a predominately rural state adds to the limited previous research on engaging healthcare personnel in HPV vaccination promotion efforts in the rural U.S.

5.6 Conclusion

In large, principally rural states like Montana, nurses and medical assistants play a key role in adolescent immunization delivery and often serve as the sole immunization providers in medically underserved areas. Because of the need to increase HPV vaccination rates to prevent HPV-caused cancers; the importance of providers' vaccine recommendations; utilizing all clinic visits as opportunities to vaccinate; and understanding healthcare personnel's knowledge, attitudes, and professional practices regarding the HPV vaccine are crucial for developing effective interventions focused on improving the consistency and strength of vaccine recommendations. Future studies should explore designing and employing novel approaches to tap into the potential of the existing workforce who are endowed with the required skills and harness their expertise in HPV vaccine promotion.

5.7 References

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Chapter: 6 A qualitative study on public health nurses' experiences and perceptions with human papillomavirus (HPV) vaccination in Montana

6.1 Abstract

Context: Human papillomavirus (HPV) is the most common sexually transmitted infection in the U.S. Despite the availability of a safe and effective HPV vaccine to prevent these infections, vaccination rates have remained sub-optimal. To design effective evidence-based strategies, a robust understanding of the facilitators of HPV vaccine delivery systems, particularly in rural and underserved areas, is crucial.

Objective: This study aimed to identify multi-level factors that influences HPV vaccine uptake among eligible adolescents within rural public health departments and delineate any strategies that high-performing public health departments implement to efficiently vaccinate age-eligible adolescents in their communities with the HPV vaccine.

Design: We conducted in-depth, semi-structured exploratory interviews with 21 immunization nurses. Transcripts were reviewed independently by two interviewers and analyzed to identify key themes.

Participants: Immunization nurses working in rural public health departments in Montana who were in the top and the bottom quartiles for the proportion of missed opportunities to vaccinate against HPV, according to state data.

Results: Interviews with 21 nurses revealed that greater parental vaccine hesitancy with the HPV vaccine and vaccine communication styles influenced HPV vaccine uptake among adolescents seeking care at rural public health departments. Participants highlighted the need to engage adolescents through tailored vaccine messaging, create training opportunities for nurses in vaccine conversations, invest in

social media campaigns, encourage collaborations with schools and community organizations, and promote HPV vaccination at every patient encounter.

Conclusions: Public health nurses play a key role in adolescent immunization services delivery in rural areas. Identifying vaccination strategies implemented by higher-performing public health departments is critical for informing future initiatives.

6.2 Introduction

The 2018 President's Cancer Panel report encouraged providers to strongly recommend and administer the HPV vaccine to age-eligible adolescents at every clinic visit to eliminate missed opportunities for preventing HPV infections and HPV-attributable cancers.[1] Despite mounting evidence shedding light on the safety and effectiveness of the HPV vaccine in reducing HPV-related genital lesions, precancers, and cancers[2-5], only 61.7% of U.S. adolescents were fully vaccinated by age of 17 years in 2021.[6] This vaccine uptake rate is well below the recommended Healthy People 2030 goal of 80% coverage.[7] Moreover, pronounced differences in HPV vaccine uptake by metropolitan statistical areas exist, with rural areas reporting lower HPV vaccine coverage when compared to their urban counterparts.[8-10] Rural communities in the U.S. also face a higher burden of health disparities related to HPV-attributed cancers. Epidemiologic analysis of the national cancer registry data from 1995-2013 reported a slightly elevated incidence of combined HPV-attributable cancers in rural populations [RR=1.07, 95% CI= 1.06-1.09].[8] Additionally, previous assessments of the urban-rural disparities in nationwide HPV vaccine coverage have demonstrated that rural females were less likely to finish the HPV vaccine series, and rural boys had lower odds of vaccine series initiation and completion when compared to their urban counterparts.[9,10]

The National HPV Vaccination Roundtable Coalition has encouraged researchers to develop and test interventions aimed at increasing HPV vaccine uptake in rural areas as a top priority to bridge the disparity in HPV vaccine utilization.[11] A robust understanding of the factors associated with lower uptake in rural areas is imperative to guide successful public health programs meant for reducing the HPV-attributable cancer burden among rural inhabitants. Previous research has identified multiple factors that are associated with lower vaccine coverage in rural areas. For example, rural residents are less likely to be aware of HPV or the HPV vaccine; possess negative attitudes toward the HPV vaccine that are strongly influenced by misinformation; experience greater transportation, and other health services access-related barriers; and are less likely to have received strong and consistent recommendations for the HPV vaccine from their providers.[12-15] On an organizational level, rural healthcare practices face greater logistical issues with stocking and storing the vaccine, experience staffing shortages, and lack training opportunities.[16,17] While most research involving adolescent vaccine delivery systems in rural areas has focused on private clinics, rural adolescents are highly reliant on public health facilities for their immunization needs.[18,19] About 20% of the US population resides in rural areas and rural adolescents frequently take advantage of public facilities to protect themselves from vaccine-preventable diseases.[20] Given the crucial role played by public health departments in maintaining community levels of vaccination, the National Vaccine Advisory Committee has emphasized the need to address barriers to vaccination in venues outside of traditional primary care provider offices, including public health departments.[21]

The promotion of HPV vaccination in a public clinic setting varies significantly from other settings like private clinics, through which older children and adolescents receive a range of routine preventive health services from primary care providers. Public health departments often offer walk-in services and are usually sought for episodic care like vaccinations. By participating in the federal

Vaccine for Children (VFC) program, public health departments can serve as a safety net for adolescents who are uninsured or under-insured to receive life-saving vaccinations.[22] In public health departments, immunization nurses regularly interact with parents and families to provide education and other services, unlike private clinics where physicians at the helm of providing health services.[23] Robust knowledge of how public health nurses fit within the larger goal of improving HPV vaccination rates will facilitate the design and deployment of effective evidence-based strategies in health departments that operate in rural and medically underserved areas.

In Montana, a predominately rural, under-resourced, and underserved part of the U.S., the rate of tetanus-diphtheria-acellular pertussis (Tdap) vaccinations, which is required in vast majority of states for school attendance, in 2021 was 88.8%, whereas only 75.3% of the adolescents had received the first dose of the HPV vaccine, signaling that teens are experiencing missed opportunities to get vaccinated against HPV.[24] Furthermore, in a statewide quantitative analysis, we found that not only were the odds of experiencing a HPV missed opportunity higher in rural as compared to urban areas [aRR: 1.12; 95% CI: 1.09-1.14], but adolescents who had received their immunizations at a public health department as compared to a private clinic were 25% more likely to not receive a dose of the HPV vaccine during the visit [aRR: 1.25; 95% CI: 1.22-1.27].[25] Through our current study, our aim was to identify multi-level factors that influences HPV vaccine uptake among eligible adolescents within rural public health departments and delineate any strategies that high-performing public health departments implement to efficiently vaccinate age-eligible adolescents in their communities with the HPV vaccine.

We identified rural public health departments in Montana with the highest and the lowest rates of missed opportunities for HPV vaccination using a positive deviance approach. Immunization nurses working at these public health facilities were invited to participate in semi-structured qualitative

interviews to elicit their perspectives on multi-level barriers to and facilitators of recommending and administering the HPV vaccine.

6.3 Methods

We used a positive deviance approach (PDA) framework to inform the selection of study participants (Figure 6.1). [26,27] The positive deviance approach is described in detail below.

6.3.1 Participants: We considered a clinic visit to be a missed opportunity to vaccinate if other recommended vaccines (Tdap, meningococcal, and influenza vaccines) were administered, but the HPV vaccine series was not initiated.[29,30] In a previous study, we used ImMTrax (Montana's immunization information system) data to quantify the proportion of missed opportunities to initiate the HPV vaccine series for adolescents who had at least one immunization record in ImMTrax and received immunization at a rural public health department. We analyzed all unique encounters for individuals who turned 11 years old between January 2014 to December 2017. We excluded individuals who had received their first dose of the HPV vaccine before their 11th birthday, and individuals with discrepancies in their vaccination records.[31]

For this study, we ranked rural public health departments from the highest to the lowest proportion of missed opportunities and stratified them into quartiles. Rurality was determined based on the county in which the public health department was situated using the Office of Management and Budget's (OMB) urban rural classification scheme.[65] Under this classification, we designated Metropolitan Statistical Areas as core urban areas of 50,000 or more population, and a Micropolitan Statistical Area as an urban core of at least 10,000 (but less than 50,000) population. All counties that are not part of a Metropolitan Statistical Area (MSA) were considered rural. Public health departments located in counties designated as micropolitan or non-metropolitan statistical or rural areas met the

sampling criteria.[65] To ensure that participating nurses from eligible public health departments had substantial experience with educating, recommending, and administering the HPV vaccine, public health departments with immunization records on a total of less than 30 adolescents were excluded. Using a positive deviance approach (Figure 6.1), we sampled 12 public health departments with lower missed opportunities and 11 public health departments with higher missed opportunities to vaccinate against HPV.

6.3.1.1 Positive Deviance Approach: The positive deviance (PD) approach framework postulates that knowledge about strategies is available in existing organizations that demonstrate consistently exceptional performance despite having access to the same resources and facing similar challenges as their peers.[26,27] The PD Approach attempts to flip the narrative that for solving complex problems within a community, external expertise must be sought. Instead, the PD approach seeks to identify internal change agents within the community.[27] The PD approach argues that often times obvious solutions to highly intractable, persistent problems within a community remains unnoticed especially by an external expert operating within the limitations of "trained incapacity"- a state where one's expertise, trainings, and abilities act as constraints.[28] Therefore, the PD approach proposes relying on professionals that possess extraordinary wisdom and pioneers of innovative solutions for prevalent problems and then amplifying it in a systematic process that leads to radical but sustainable organizational and community transformation. Historically, the positive deviance approach has been successfully implemented in 50 countries to find innovative solutions to complex social and healthcare problems.[27] For example, in Vietnam, to solve the rampant issue of malnutrition among young children, U.S. researchers effectively implemented the positive deviance approach by seeking strategies from caregivers/parents of children thriving in poor households.[27] By following simple techniques like supplementing food with inexpensive and accessible protein and micronutrient sources, increasing the

frequency of daily meals consumed by children, and practicing active feeding to eliminate food wastage, families with scarce means were able to avoid malnutrition without access to any special resources. Other instances where the PD approach was successfully applied to achieve favorable health or social outcomes are reducing school dropout rates in Argentina,[27] reducing female genital mutilation in Guinea,[32] reducing neonatal and maternal mortality in Pakistan,[33] reintegrating returned child soldiers in Uganda and Indonesia,[34] and enhancing female entrepreneurship in India's rural areas[35]. In the United States, the PD approach has been extensively used to reduce hospital-associated infections, improve care for patients recovering from myocardial infarction, and overcome access to care challenges in community health centers.[36-38]

The Positive Deviance approach recommends that innovative solutions should be based in local resources to ensure scalability by enabling easy adoption by other community members and sustainability in the long run.[39] As identified by Bradley and colleagues, the PD approach can be effectively implemented in situations where there are existing concrete; widely endorsed, and accessible measures for organizations to compare performance; organizations can be ranked based on pre-selected performance and outcome measures; the hypotheses generated from the experience of top performing organizations can be tested in larger, representative samples; and potential implementers and stakeholders perceive the solution to improve performance measures to facilitate dissemination of best practices.[39]

The application of positive deviance approach begins with delineating the problem and defining precise measures that will be used to rank performance of individuals/organizations. This is followed by discovering uncommon but replicable behaviors and practices prevalent among exceptional performers to design successful interventions for potential adopters. The effectiveness of the interventions is monitored regularly and then disseminated across communities. (Figure 6.1)

Based on the principles governing the successful application of the PD approach, we believe that using a PD approach for determining our study sample was appropriate. In terms of utilizing concrete, well-established measures to compare performance between public health departments, we relied on immunization data obtained from Montana's immunization information system. Second, the positive deviance approach works when there is variation in organizational performance and outcomes across the industry, with some organizations achieving marked and consistent top performance and other organizations not doing so, *i.e.*, there are positive deviants. For our study sample, we ranked the public health departments based on the proportion of clinic visits that were missed opportunities to initiate the HPV vaccine series and selected public health departments with higher and lower HPV missed opportunities.[39]

6.3.2 Recruitment: After obtaining approval from the University of Montana Institutional Review Board, we sent emails to eligible immunization nurses working at sampled public health departments introducing the study and requesting to schedule a 45-50 minute interview. Emails contained a brief study description, the study investigator and collaborator's information, incentives, and directions on how to schedule the interview. We conducted follow-up phone calls to nurses, who did not respond to the initial email communication, to answer questions, and to assess their willingness to participate in the study.

6.3.3 Data Collection: Immunization nurses who agreed to participate in the study were asked to answer a short survey questionnaire two days prior to the scheduled interview. The purpose of the survey questionnaire was to develop a rapport with the nurses and to familiarize them with the overall study goals. The survey questionnaire was developed on an online data collection platform and had a total of five questions; four practice and participant related questions and a concluding question on HPV vaccination practices implemented at the facility. This was followed by in-depth interviews using

a semi-structured interview guide. The semi-structured nature of the interview guide permitted greater flexibility in responding with additional probes to new and unexpected responses.[32] The questions in the interview guide were developed based on existing literature on multi-level barriers to and facilitators of HPV vaccination and study objectives.[33-36] Questions were divided into three distinct sections to identify the patient, provider, and practice-level factors that influence adolescent immunization delivery systems, with a particular focus on HPV vaccine delivery (Appendix i). All the interviews were conducted by one coauthor (J.T.) on a virtual platform from 07/13/2022 to 08/31/ 2022, were audio and video recorded, and ranged from 35-60 minutes in length. Participants provided their consent before answering the survey questionnaire and the interview questions. The data collection instruments were pretested with four nurses working at non-participating public health departments. The complete interview guide is available in the supplementary section. Nurse participants were awarded a $50 gift card as an appreciation for their time and participation.

6.3.4 Data Analysis: We used the Consolidated Framework for Implementation Research (CFIR) constructs to guide our initial deductive data analysis. The CFIR offers an overarching list of constructs to promote theory development and verification about what works where and why across multiple contexts.[40] The CFIR construct identifies five major domains of organizational context that influences the successful implementation of intervention; the characteristics of the intervention, the inner setting (the context through which implementation will proceed), the outer setting (the context in which the organization resides), the implementer's characteristics, and the processes involved in the implementation.[41] These domains interact in rich, complex ways to influence implementation effectiveness. The CFIR guidelines have been extensively used to develop data collection approaches (e.g., interview guide, codebook) and also as a guide for analyzing, interpreting, and/or reporting findings.[42]

We created a preliminary codebook using the CFIR domains and their constructs, and the interview sections. We transcribed the interviews verbatim using third-party transcription services (GoTranscript©) and uploaded them on NVivo© for data analysis.[43] Participant identifiers on transcripts were replaced with unique study identifiers to maintain the confidentiality of participants' responses. Two researchers (J.T. and T.A.) independently performed a content analysis on a subset of transcribed interviews (n=6) using a deductive approach to identify emerging themes that accurately fit the code definitions.[44] Using an iterative approach to coding, researchers (J.T. and T.A.) met for weekly briefings to discuss the coding scheme. The codebook and the emerging themes and subthemes were refined using an inductive process until a consensus was reached. The remaining transcripts were analyzed by J.T. using specific code and subcode definitions listed in the codebook. We selected exemplary quotes from the nurse participants to present along with the study findings. The study results were presented at the 2023 Montana Public Health Association Meeting, the Intermountain West HPV Vaccine Coalition monthly meeting, and the annual Cancer Epidemiology Education in Special Population meeting. We followed the SRQR guidelines to report the study findings.[46]

6.4 Results

Participant Characteristics: Our study sample consisted of a purposive, stratified sample of 21 public health nurses; 12 were from the departments that reported lower rates of missed opportunities and 9 were from departments that reported higher rates of missed opportunities. Relatively fewer nurses in either group refused participation (n=3). The proportion of missed opportunities among public health departments in the higher-performing group ranged from 41.7%-58.0% and for those in the lower-performing group ranged from 75.5%-93.7%

Details on the provider characteristics, organizational workforce, and immunization practices are presented in Table 6.2. The majority of nurse participants identified themselves as females and

white and reported having less than 5 years of experience as a public health nurse. Participating nurses represented about 43% of the counties in Montana.

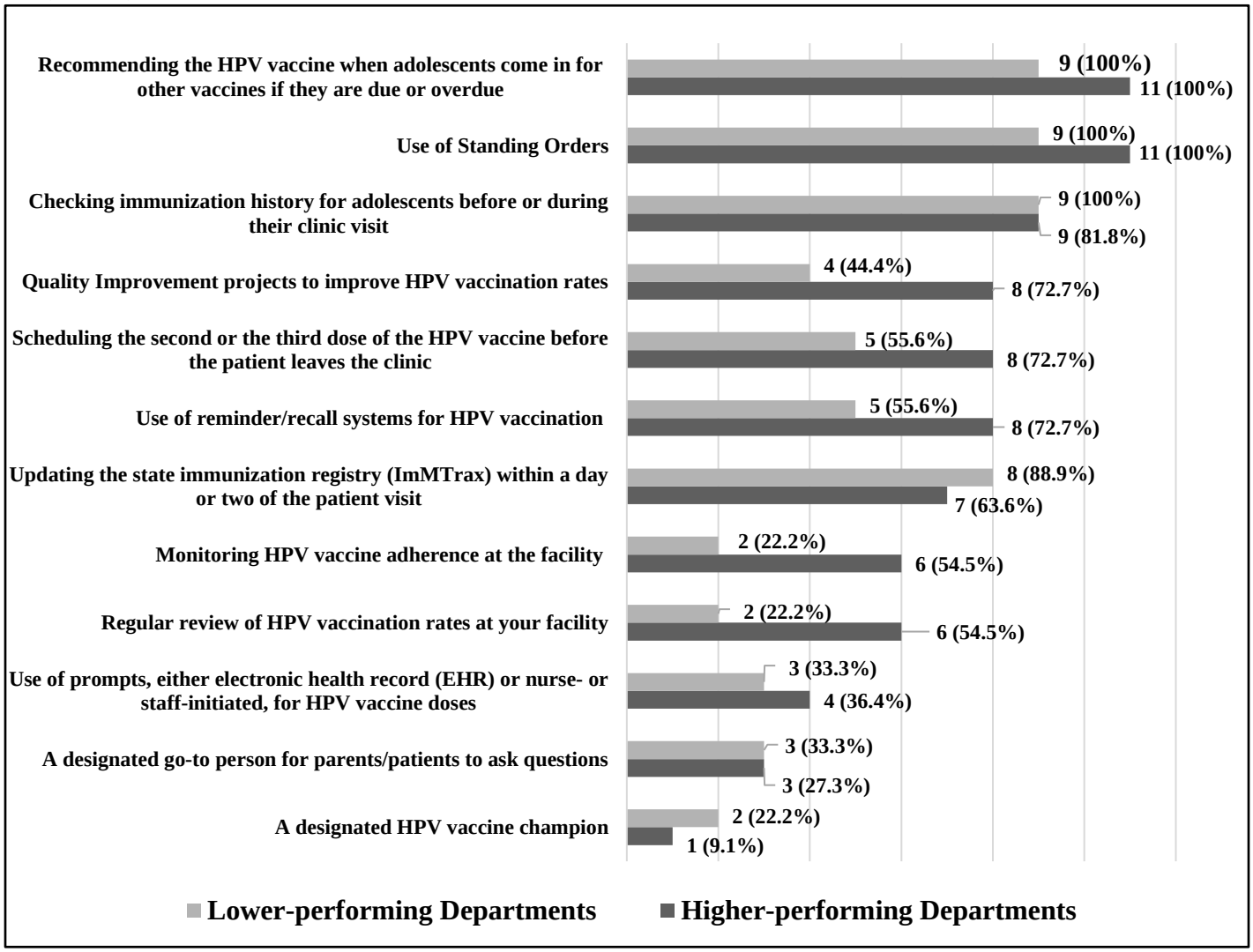
We have summarized the study results as barriers to and facilitators of recommending and administering the HPV vaccine as reported by the study participants in Table 6.3.

Table 6.1: Provider and practice characteristics

	N (total=21)	%
Nurses' Age		
Less than 40 years	9	42.9
41-60 years	8	38.1
More than 60 years	4	19.0
Experience as a nurse		
Between 6-9 years	2	9.5
More than 10 years	11	52.3
More than 20 years	8	38.1
Experience as a public health nurse		
Less than 5 years	9	42.9
Between 6-9 years	4	19.0
More than 10 years	5	23.8
More than 20 years	3	14.3
Full-time staff members employed at the facility		
Less than 5 employees	16	76.2
Between 6-10 employees	3	14.3
More than 10 employees	2	9.5
Part-time staff members employed at the facility		
None	8	38.1
Less than 5 employees	11	52.3
Between 6-10 employees	1	4.5

Findings from the short survey questionnaire: Figure 6.2 summarizes the responses received through the short survey questionnaire that was administered to the participating public health nurses. As shown in Figure 6.2, all public health nurses that completed the questionnaire reported using standing orders to recommend the HPV vaccine along with other recommended adolescent immunizations. More nurses in the higher performing group implemented quality improvement projects related to the HPV vaccine at their facilities (n=8,72.7%) as compared to nurses working at lower-performing public health departments (n=4,44.5%). With regard to using reminder-recalls to inform parents/patients of vaccinations that are due or overdue, more nurses in the higher performing group (n=8,72.7%) reported conducting reminder-recalls at their facilities as compared to nurses in the lower performing group (n=5,55.6%). Fewer nurses in the lower performing departments reported having a process to regularly review HPV vaccination rates or monitor HPV vaccine adherence at their facilities (n= ,22.2% v/s n=, 54.5%). Very few nurses, regardless of the group, reported having a designated HPV vaccine champion (n=3, 15.0%) or a 'go-to' person to ask questions about the HPV vaccine. (n=6, 30.0%)

Figure 6.2: HPV vaccination clinic practices by public health department type (N=20)*



*****Since two nurses from the same public health department participated in the interview, we used responses from only one completed questionnaire.

Findings from qualitative interviews:

A differentiating theme between nurse participants working at public health departments with lower proportions of missed opportunities compared to those working at a public health facility with higher proportions of missed opportunities was their vaccine recommendation styles. Nurses in the higher performing group adopted more of an "announcement/presumptive" approach, nurses in the lower-

performing departments adopted a conversational/participatory style to present the HPV vaccine to patients and their parents. Also, nurses in the lower-performing departments more often presented the HPV vaccine as “recommended” but “not required”. We did not find other major differences in HPV vaccination practices among higher performing and lower performing public health departments that could be contributing toward HPV vaccine uptake disparity. The majority of nurse participants expressed an overwhelming interest in identifying ways to engage parents and patients in HPV vaccine promotion. One of the public health nurses underscored the importance of leveraging social media to spread awareness about the HPV vaccine and to debunk misinformation, especially in predominately rural areas with limited access to resources.

Intervention Characteristics: Some common discussion themes that nurses regularly employed in their interactions while counseling parents and patients about the HPV vaccine included cancer prevention, the prevalence of HPV-associated infections, the gender-neutral nature of the vaccine, and the necessity to get vaccinated before sexual debut. In fact, one nurse practitioner noted that changing the narrative from “HPV vaccine prevents sexually transmitted diseases” to “HPV vaccine prevents cancer” has encouraged her patients to be more receptive. The greatest benefit to using simpler terms like cancer prevention as observed by one study participant in their practice is that it resonates well with parents across varied socio-demographic backgrounds. The multi-dose nature of the HPV vaccine was identified by several nurses as a barrier that increases the complexity of administering the HPV vaccine as per the recommended guidelines.

While most nurses affirmed their confidence in their ability to counsel vaccine-hesitant parents on the benefits of HPV vaccination, some expressed frustration about the lack of training opportunities in vaccine conversations spot provide strong and consistent vaccine messages tailored for public health nurses. A nurse practitioner said,” No because if I was up to date, I would not likely be lost in my

conversation with parents." Another nurse echoed, "I think our biggest barrier is trying to get them (parents) the right information but in the proper way without the argument side of it."

The cost of administering the HPV vaccine was not identified as a barrier by study participants. Stressing the importance of getting vaccinated at the right age, nurse participants would either "offer a sliding scale", "use donations" or "write off the amount completely" so that they do not have to "turn away" uninsured individuals who do not otherwise qualify to receive free vaccines under the federal Vaccine for Children program.

Table 6.2: Barriers to and facilitators of adolescent human papillomavirus (HPV) vaccination, identified from qualitative data collected from public health nurses (n=21), Montana organized by the Consolidated Framework for Implementation Research Framework

	Barriers	Facilitators
Characteristics of Intervention (use of the HPV vaccine as per the stipulated guidelines	a) Multi-dose vaccine	Ensure greater vaccine acceptance by: a) Emphasizing cancer prevention b) the gender-neutral nature of the vaccine c) importance of getting vaccinated before initiating sexual activity
Outer Setting	Lack of state laws: a) Mandating the HPV vaccine for school entry Negative influences on parental vaccine attitudes due to: a) Vaccine critical information received from social media b) friends, family members, peers	School-based collaborations to: a) spread awareness about the HPV vaccine b) provide routine and catch-up vaccinations State policies to improve access: a) the federal "Vaccine for Children" program b) state sponsored Montana Teen Vax program c) CareVan© program
Inner Setting		Access to resources through the: a) state immunization information system (IIS) b) the state health department Improve follow-through using: a) reminder-recall processes

		b) scheduling the subsequent doses before the patient leaves the clinic
Characteristics of participants	Beliefs about ownership: a) Primary care physicians' role in increasing community demand for the HPV vaccine	Positive perceptions about the HPV vaccine: a) confidence in vaccine safety and efficacy b) self-efficacy in providing strong recommendations
Process	Perceived need: a) optional vaccine not needed for school entry Parental/patient engagement: a) need for eye-catching promotional materials in addition to the VIS	Approach toward vaccine recommendation: a) using a bundled approach b) making a recommendation in the next visit even if refused in the past

Outer Setting: A number of nurses reported that as compared to other vaccines, parents expressed greater vaccine hesitancy with the HPV vaccine which directly translated to a greater number of vaccine refusals. Several nurses pointed out that since Montana laws do not mandate the HPV vaccine, it is the most commonly deferred or refused vaccine among adolescents. Parental perceptions that the HPV vaccine causes fertility issues, encourages early sexual activity, teens are too young to receive the HPV vaccine, misconceptions that the vaccine only protects against cervical cancer and thus not recommended for boys, and the HPV vaccine being a relatively newer vaccine might not be safe or efficacious were cited as some of the commonly encountered barriers to the HPV vaccine. Most nurses felt that misinformation from social media, friends, families, and peers fueled the vaccine hesitancy, particularly related to the HPV vaccine, among community members.

Stressing the importance of provider recommendations, one nurse noted that consistent vaccine recommendations from all health providers in their community had eventually reduced the pushback

they received from parents. Interestingly, one nurse practitioner provided an anecdotal view that she receives less pushback from parents while recommending the HPV vaccine to a male patient as compared to a female patient because parents are more comfortable with the idea that their sons will engage in sexual activity at some point in their lives. All the participating nurses emphasized that there is a need to improve access to the HPV vaccine and make it easier for parents to get their age-eligible children vaccinated with the school-required (Tdap) as well as other recommended vaccines (Meningococcal, HPV). Most public health nurses reported frequently collaborating with schools in their communities to conduct spring and fall vaccination clinics. Collaborating with schools gave the nurses an opportunity to identify adolescents that are due or overdue to receive their vaccinations. However, a few public health nurses reported facing resistance from school administration to engaging parents and teens in vaccine promotion, particularly the HPV vaccine due to political reasons. Nurses unanimously agreed that school-based vaccination drives offer a convenient option for parents to ensure up-to-date vaccination status for their children. Emphasizing on the need for offering a flexible schedule to accommodate parents, one of the nurses offered vaccination appointments during lunch breaks while some others collaborated with the Blue Cross Blue Shield of Montana's Care Van© program to offer vaccines on-site in schools. The Care Team, through the Care Van program, provides vaccines, health screenings, educational resources, and preventive services across Montana with a special focus on rural and frontier counties.[47] Very few nurses opined that funding cuts and staffing shortages curtailed their availability for vaccine conversations with their patients and invest in quality improvement projects or promotional strategies for vaccines within the facility.

Inner setting: ImMTrax is Montana's immunization information system. Nurses reported regularly using ImMTrax to review patients' immunization history; conduct reminder-recall for patients that are due or overdue to receive vaccine doses; order, and stock vaccines through the VFC program; update

the visit summary; run reports periodically to evaluate the immunization rates at their facilities or community; and share immunization records with patients. One nurse participant reported using built-in provider prompts in the electronic medical records system to identify vaccinations that are due or overdue for every clinic visit.

To ensure that adolescents complete their HPV vaccine series, all nurses reported using some form of reminder-recall processes at their facilities. However, the mode and frequency of conducting the reminder-recall differed. Some nurses preferred to call the patient about four weeks in advance to inform them that they were due to receive their vaccine dose while some preferred to send a mail suggesting that the parent or the patient schedule an immunization appointment with them. One of the nurse participants pointed out that doing reminder-recall was not cost-effective and they preferred to administer vaccinations during school vaccination drives while two other nurses identified lack of resources, manpower as barriers to conducting regular reminder-recalls. Most nurses in the higher-performing group ensured that parents and patients had scheduled an appointment for subsequent HPV vaccine doses before checking out while more nurses in the lower-performing group asked the patients to call the facility at a later time to schedule an appointment for successive doses of the HPV vaccine.

Nurses referred to diverse external resources to obtain latest vaccine-related information. Nurses routinely checked the Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices (ACIP) websites to stay up to date on vaccine recommendations Other resources that nurses frequently relied on to obtain HPV vaccine-related information included websites like immunize.org, Ask the Experts, the Immunization program section within the Montana state health department, Moffitt Cancer Center, the Children's Hospital of Philadelphia, the Mayo clinic, and American Academy of Pediatrics. Considering the time required to actively search for specific information online, nurses stressed that receiving health research information via emails, newsletters or

webinars facilitates greater engagement and reach. Additionally, one of the nurses emphasized the need for regular training opportunities on vaccine communication strategies.

When asked about sharing vaccine-related research, new information, or toolkits among staff members, about half of nurse participants reported having both formal and informal communication channels within the facility. For example, while the majority of the nurses reported having informal hallway conversations with other staff members, a few nurses mentioned that they either schedule regular meetings with health providers across the county or shared information through emails.

The CDC encourages providers to implement quality improvement projects to bring about measurable improvements in HPV vaccination rates.[48] Some quality improvement projects that nurses routinely participated at their facilities included the state facilitated Immunization Quality Improvement for Providers (IQIP) program and the Montana TeenVax challenge. The IQIP program encourages the providers to give strong vaccine recommendations, schedule the next visit before the patient leaves the clinic, and conduct regular reminder-recalls,[48] while the Montana TeenVax challenge offered a small incentive to adolescents who received all doses of recommended vaccines.[49] However, a few nurses expressed disagreement with offering gift cards or other monetary compensation in exchange for vaccination and thus were not keen on participating in the Montana TeenVax challenge.

Other strategies to increase HPV vaccine use included stocking educational materials like posters in the clinic waiting rooms, schools or other public places, informational booths at community events, using social media including newspapers to spread positive messages promoting vaccination, sharing personal narratives, and providing educational materials to engage adolescents. None of the nurses reported facing logistical issues with ordering or stocking vaccines through the VFC program or directly from the pharmaceutical companies. However, one nurse reported facing challenges with vaccine waste due to expired doses.

Process: Nurses typically recommended the HPV vaccine at the 11-12-year old well child visit and bundled the HPV vaccine along with the Tetanus, diphtheria, and acellular pertussis (Tdap) and the meningococcal vaccine. Nurses used the same approach for girls and boys. Nurses routinely did not recommend the HPV vaccine to 9-year-olds as they anticipated receiving greater parental pushback. To encourage vaccination, nurses ensured that they provided vaccine recommendation for at least two subsequent visits even to parents that had refused the vaccine in the previous visit. However, more nurses in the lower-performing group were hesitant to "push" the HPV vaccine for the fear of adversely affecting the provider-patient relationship. Nurse participants routinely shared Vaccine Information Statements (VIS) with their patients and patients. Promotional materials from the pharmaceutical companies and CDC's website were other resources that nurse participants routinely referred their patients to seek more information on the HPV vaccine.

When enquired about the effects of the COVID-19 pandemic on the vaccination rates in their communities, most nurses acknowledged that community vaccination rates had plummeted since the pandemic due to growing mistrust in the government and other public health agencies and rising vaccine hesitancy. Even though a majority of the nurses offered the HPV vaccine along with the COVID-19 vaccine at their facilities, not many parents opted to receive the HPV vaccine along with the HPV vaccine due to safety concerns.

Characteristics of Individuals: All participating nurses demonstrated strong support for the HPV vaccine stemming from their confidence in the safety and effectiveness as emphasized in the following quotes, "we know it works and we know it's safe", "I think that it's something that can save lives". To further exemplify their trust in the safety of the HPV vaccine, some nurse participants routinely shared personal stories of their children getting the HPV vaccine with their patients. Additionally, while the majority of the nurses indicated that they never had concerns with recommending or administering the

HPV vaccine to their patients, one participant expressed that she experienced some nervousness because of non-serious adverse event like fainting following administration being common with the HPV vaccine. Greater faith in vaccines, higher vaccination rates, lower rates of HPV-associated infections and precancers, and increase in parental knowledge of HPV and its role in cancer prevention were some responses that nurses provided when asked about health outcomes they would like to see improved in their communities because of an educational intervention. All but one nurse participant affirmed that they were confident in their abilities to strongly recommend the HPV vaccine and counsel vaccine hesitant parents.

Most of the strategies to improve HPV vaccination rates reported by public health nurses were focused on parental education and reengagement through community outreach, facilitating regular check-ins and discussions between different public health departments. creating training opportunities in vaccine conversations for nurses, designing eye-catching promotional materials, and investing in expansion of public health workforce. Table 6.3 presents illustrative quotes for each domain and subdomain under the CFIR model.

Table 6.3: Consolidated Framework for Implementation Research domains, constructs, and illustrative quotes

Domains	Constructs	Representative Quotes
Innovation Characteristics	**Adaptability**	**“** When they come in for their 11-year-old shots with their Tdap and meningococcal, we always tell them, "This is what the Academy of Pediatrics, this is what general recommendations are."
	Cost	**“**We usually find a way to make it work so that's not a barrier for them because I know it's a very expensive vaccine.”
	Complexity	“A lot of times, kids pass out with the HPV vaccine. I don't know if this gives more vasovagal reaction or just the pain of it, I don't know exactly, but every time I give an HPV, I'm thinking, "Oh this kid may pass out."

Inner Setting	**Available Resources**	"We look up their immunization status on ImMTrax. Without ImMTrax, it's nearly impossible to keep up, so we're really grateful for ImMTrax."
	Relative Priority	"Well yes and of course it has. There's just only so much time in the day and sometimes it's easier to-- Instead of thoroughly discussing HPV vaccine. We'll say maybe one or two things and then let it go, because we just don't have time for the battle."
Outer Setting	**Needs and Resources of those served by the organization**	"Yes. Some I do see that all they [*parents*] needed was more information and they were willing to do it " "Some *[Misconceptions about the HPV vaccine]* is social media, some is from other family members, but probably most of it is from social media."
	Cosmopolitanism	"We had trouble getting into the school last year to do any public health teaching training. This is the first year that I've actually had hands-on in the school. I feel like I'm starting to build that relationship and seeing, I guess, which ones are the risky behavior, which ones aren't prior to that everybody was equal."
Characteristics of Individuals	**Knowledge and Beliefs about the Innovation**	"I think it's very important. Number one, for women, it could almost eliminate cervical cancer, which has been a scourge on our ladies. In addition to that, there are so many other cancers that are now being linked to it."
	Self-efficacy	"Like I said, I went to one training on HPV specific, and that's not enough to then turn around and be able to talk to somebody else about it. Training to us is always important because unfortunately, right now, seeking out my own training just takes too much time."
Process	**Executing**	"They come into registration. They usually book an appointment or if they're a walk-in we just get their name and then all of our stuff is paperwork. Still paper, nothing's digital yet. Usually, we give them the VIS sheet. If it was for immunization, we'd give them the VIS sheet. I sit down I talked to them, "This is what your kiddos going to get." Explain everything and then ask if they have any questions. If they don't have questions then I let them fill out the rest of the paperwork and then I go ahead and give them their shots."
	Engaging	"We do quite a bit of communication in our community through Facebook messenger and personal texts just because it's a small community and everybody knows everybody."

Vaccine Recommendation Styles	**Presumptive Approach**	"Today you can have Tdap, MCV4, and HPV." I just mention HPV like any other vaccine, like I will mention a Tdap or a Hep A or any other vaccine"
	Participatory Approach	"Then if there's anything extra, like HPV is typically an extra one on the seventh-grade shots, that I try to encourage people to get. I will say, this is what they have to have for school, they need to Tdap, they need their meningitis"

6.5 Discussion

Public health departments play an integral role in educating the community and reinforcing trust in vaccines to maintain higher levels of community immunization rates. In this study, we examined multi-level factors that influence the uptake of the HPV vaccine in rural communities within the domains of the Consolidated Framework of Implementation Research. Interviews with 21 nurses revealed that greater parental vaccine hesitancy with the HPV vaccine as compared with other vaccines and vaccine communication styles influenced community HPV vaccination rates. Nurse participants also highlighted the need to engage adolescents and their families through tailored vaccine messaging, create training opportunities for nurses in vaccine conversations, invest in social media campaigns, encourage collaborations with schools and community organizations, and promote HPV vaccination at every patient encounter. Our study findings facilitated the identification of potential strategies for promoting HPV vaccination in rural communities that can bridge the urban-rural disparity in vaccine uptake.

Our study findings indicated significant differences in vaccine recommendation styles between public health nurses in the higher-performing and the lower-performing groups. Previous research has consistently shown that providers' recommendation style is as influential as the recommendation strength on parental vaccine decisions.[67-69] For example, providers that presented the HPV vaccine as

one of the several other vaccines using the same way same day approach and provided strong recommendations faced lesser vaccine hesitancy and higher vaccine uptake.[70] On the other hand, when providers presented the HPV vaccine as being 'optional' and not required for school entry faced greater parental hesitancy leading to vaccine deferral or refusal and lower vaccine uptake. Additionally, parents that delayed the vaccination with the intention of getting the vaccine later reportedly did not follow-up.[70,71] In our study, we found that nurses in the lower-performing departments often separated the HPV vaccine from other routine vaccines while presenting it to parents and patients and referred to the HPV vaccine as being a "recommended" instead of a "required" vaccine. contributing to higher parental vaccine hesitancy and missed opportunities at these facilities. Additionally, nurses in higher performing departments regularly used the announcement approach presenting the vaccine with a presumption that parents intend to vaccinate their children with the HPV vaccine whereas nurses in the lower performing often used a participatory approach. Use of 'presumptive' or "announcement" approach has been widely endorsed by researchers to achieve greater parental vaccine acceptance and has shown to significantly increase series initiation and completion rates.[68,72,73] Despite the obvious benefits of using specific communication strategies on studies have found that providers inconsistently used these best practices in vaccine communication during their interactions with parents or patients.[61] In fact, nurse participants from our study acknowledged that there are fewer vaccine communication training opportunities specifically geared toward nurses working in rural public health departments. Programs to improve HPV vaccine delivery should focus on promoting effective parent-clinician communication.

Parental vaccine hesitancy was identified by public health nurses as the most encountered barrier to HPV vaccination in rural areas. As defined by the World Health Organization, parental vaccine hesitancy is a set of behaviors influenced by a number of factors including issues of confidence

in the vaccine or the provider, complacency, and convenience.[50] Socio-political changes and growing mistrust resulting from the COVID-19 pandemic might have had spill-over effects on parental acceptance of other vaccines.[61] For example, a paper assessing parental vaccine hesitancy that was published in the year 2021, researchers found that one in five parents of adolescents were hesitant about adolescent vaccinations, and parental vaccine hesitancy was associated with significantly lower coverage for HPV vaccination among adolescents; ranging from 18% to 24% lower coverage for HPV vaccine series initiation and completion, respectively, among adolescents with hesitant parents compared with adolescents with non-hesitant parents.[51] Qualitative interviews with parents revealed that their hesitancy was driven by concerns about safety and necessity, often based on negative anecdotal reports. Parents expressed a desire for detailed information on both the benefits and risks of the vaccine, and resources that allowed them to actively participate in vaccine discussions with providers.[52] To address the existing challenges of hesitancy and refusal of the HPV vaccination, public health nurses need to be empowered with the latest knowledge and training strategies essential to assist parents in decision-making. Public health nurses could leverage their positioning and recognition in the community and take advantage of the multiple opportunities of direct contact with their patients and their parents to raise public awareness about the HPV vaccine.

Social media messaging and its influence on parental and patient HPV vaccine knowledge, attitudes, and behaviors have been extensively studied in the literature.[53-55] In our study, nurse participants noted that misinformation received from social media played a significant role in shaping parental perceptions about the HPV vaccine. Our results confirmed the findings from previous studies on HPV vaccination barriers.[62-64] In recent years, more parents are turning to social media to receive health-related information.[56] Social media has emerged as a powerful channel for either encouraging or discouraging vaccination. In a study by Kie-Malpass et al, it was revealed that most information

disseminated on social media platforms like Twitter originated from lay consumers and was not fact-checked and about 28% of websites contained information that was highly dissuasive of the HPV vaccine.[57] Consistent with these findings, Margolis et al. found that stories of HPV vaccine harms were frequently encountered on social media.[55] Dunn et al. found that among users that tweeted about HPV vaccines, those who were more often exposed to negative opinions were more likely to subsequently post negative opinions (RR: 3.46, 95% CI 3.25-3.67).[58] This is concerning considering several studies have identified a strong association between potential exposure to negative, anti-vaccine content and lower vaccination rates.[53,54] Public health nurses must increase the use of social media to the advantage of public health in the persistent struggle against vaccine hesitancy and refusal. The initial communication messaging that the HPV vaccine prevented sexually transmitted infections severely affected its uptake in the United States.[59] Results from past research have indicated that parents and adolescents are willing and interested in receiving accurate and helpful information about HPV and HPV vaccination through social media.[56] Public health nurses along with local health departments can strengthen their positions from being the mediators in immunization processes to serving as the moderators of information that is consumed by their patients.

One of the major strengths of our study findings lie in the representativeness of our study sample. By using a positive deviance approach, we were able to engage and interview about 90% of all eligible nurses from both higher-performing and lower-performing public health departments nurses. This provided us with an opportunity to dive deeper into diverse perspectives about different challenges that nurses face in their practices to adhere to recommend and administer the HPV vaccine in accordance to stipulated guidelines. Despite this, our study findings are limited in terms of generalizability to other types of clinic settings. Interviewees' responses could be subjected to social desirability bias and might not accurately represent clinic vaccination workflows and practices.[66] Since

the data collection focused on nurses only from Montana, the study findings might not be generalizable to other states. To eliminate the effects of interviewer bias on study findings, all interviews were conducted by the same interviewer (J.T.), a member of the study team who is trained in qualitative research methods. Also, we interviewed only one participant from each public health department which makes it difficult to get an exact representation of all clinical practices and workflows. We were also limited in our ability to triangulate the study findings since we did not interview parents or patients on their attitudes or perceptions of the HPV vaccine.

Implications for Policy & Practice:

a) To address current challenges related to adolescent vaccinations and assist parents in making informed decisions, public health nurses should be provided with training opportunities to access and integrate new knowledge into their healthcare delivery practices.
b) Federal and local health organizations should consider investing in social media campaigns to engage and educate parents on the essential role of the HPV vaccine in cancer prevention, particularly in rural communities.
c) School-based vaccination clinics are excellent avenues to provide routine as well as catch-up vaccinations in a timely manner. Efforts to facilitate collaborations with schools in medically underserved areas be prioritized.
d) Quality improvement (QI) initiatives can increase HPV vaccination rates. Cross-sector collaborative approach for quality improvement processes between public and private entities can ensure its successful implementation and sustainment.

6.6 Conclusion

Public health nurses are well-positioned to influence health behaviors and achieve desirable health outcomes due to their close association with community members. To facilitate significant

improvements in HPV vaccine uptake in rural areas, it is important to tap into the potential of other health providers like public health nurses and harness their expertise. Future research should seek to test the effectiveness of multi-level strategies identified in this study to improve HPV vaccine uptake in rural and medically underserved areas.

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Chapter 7: County-level sociodemographic and access-to-care factors associated with missed opportunities for HPV vaccination in a large, rural U.S. state: A cross-sectional ecologic study

7.1 Abstract

Purpose: Missed opportunities are clinical encounters when an age-eligible adolescent receives one or more recommended vaccines but does not receive the HPV vaccine. In Montana, while the rates of Tdap are higher in this age group, the HPV vaccination rates have remained lower, signaling missed opportunities. However, factors related to missed opportunities in Montana are understudied.

Methods: We analyzed Montana's immunization information system data to identify clinic visits that were missed opportunities to initiate the HPV vaccine series for adolescents who turned 11 years old in 2014-2017. Using generalized linear mixed models, we determined county-level sociodemographic and access-to-care factors that were associated with missed opportunities. Data on county-level covariates were obtained from publicly available datasets.

Results: About 53.9% out of a total of 71,447 clinic visits were identified as missed opportunities for HPV vaccination. The rates of missed opportunities exhibited a wide variation among counties ranging from 31% to 81%. After adjusting for age and gender, higher county level proportions of American Indian/Alaska Native population, children in single parent household, families receiving public assistance, the income equality ratio, and population density were significantly associated with experiencing lower odds of missed opportunities for HPV vaccination. Furthermore, increases in the percentage of rurality was significantly associated with higher odds of experiencing a missed opportunity for HPV vaccination while presenting for other adolescent immunizations.

Conclusions: Targeted interventions based on social vulnerability can facilitate effective allocation of resources to achieve vaccine equity. We found a high proportion of missed opportunities among counties that were associated with selected sociodemographic and economic factors. Results from our

study identify a need to prioritize HPV vaccine promotion efforts among populations in counties with higher rates of vaccine hesitancy.

7.2 Introduction

Human papillomavirus is the most common sexually transmitted infection in the United States.[1] So far, more than 200 unique strains of the human papillomavirus have been identified, of which 18 are known to be oncogenic and potentially cause cervical neoplasia and other anogenital and oropharyngeal cancers.[2,3] In 2018, an estimated 6.9 and 6.1 million men and women respectively had an incident infection with a disease-associated HPV type in the United States.[4] More than 90% of new infections resolve without any sequela, however, about 10% of infections persist for over two years.[5] A nationwide analysis of cancer registry data revealed that approximately 47,199 new HPV-associated cancers occurred in the United States each year from 2015 to 2019; 26,177 among women and 21,022 among men.[6] Cervical cancer is the most common HPV-associated cancer among women, and oropharyngeal cancers (cancers of the back of the throat, including the base of the tongue and tonsils) are the most common among men.[7]

The HPV vaccine protects against six different types of cancers.[8] Widespread vaccination has the potential to eliminate cervical cancer through herd effects and cross-protection.[9,10,11] In view of the evidence that the HPV vaccine is most effective when given before any exposure to the HPV virus, the CDC's Advisory Committee on Immunization Practices (ACIP) in 2006 recommended that a bivalent HPV vaccine be routinely administered to girls ages 11-12 years of age. These recommendations were expanded in 2009 to include both girls and boys. The current recommendation encourages adolescents ages 11-12 years to get vaccinated with the nine-valent HPV vaccine. ACIP also recommends vaccination for everyone through age 26 years if not adequately vaccinated when younger.[12] HPV vaccination is given as a series of either two or three doses, depending on age at initial vaccination.[12]

Since it was first introduced in 2006, the HPV vaccine has directly led to significant reductions in the prevalence of HPV-associated genital infections including high grade cervical and anal intraepithelial lesions and oropharyngeal infections.[13-17] Surveillance studies from several countries including the United States has shown that the HPV vaccine is safe.[18-20] Since the introduction of school-based vaccination programs, the HPV vaccine has significantly reduced the incidence rates of genital in countries like Australia and the UK.[21,22] However, population level reductions in cervical precancers and cancers have not been fully realized in the United States due to disparities in vaccine uptake.[23,24]

Despite the American Cancer Society and the American Academy of Pediatrics' endorsement for standing recommendation issued by the Advisory Committee on Immunization Practices, HPV vaccine uptake among adolescents in Montana has remained low.[25,26] In 2021, about 24.7% of adolescents ages 13-17 years had not received a single dose of the HPV vaccine, and 47.4% had not completed the vaccine series.[26] Similar to other U.S. states, Montana law requires that adolescents receive a booster dose of tetanus, diphtheria, and pertussis (Tdap) vaccine before entering the seventh grade. However, regarding other recommended vaccines in this age group, like the meningococcal conjugate (MCV4) and the HPV vaccine, no such laws exist.[27] Partly due to the varying vaccine mandate laws, while the rates of Tdap vaccination have increased significantly over the past years, the uptake of HPV and the meningococcal vaccine has remained low. In 2021, Tdap vaccine coverage in Montana was 90.1% among 13-17-year-old adolescents. In comparison, Montana ranked among the ten bottom-most states for meningococcal vaccination and HPV vaccine series completion rates.[26]
There is a growing interest to explore community-level factors and their influences on vaccination rates to ensure vaccine equity in public health policies. Several community-based composite indices have been extensively employed in recent times to identify vulnerable populations for the effective allocation of health resources.[28-32] For example, Saelee et al. used the Minority Health Social Vulnerability Index

(MHSVI) to examine COVID-19 vaccination rates among on a broad spectrum of social vulnerability.[29] The social vulnerability index utilized in this study was built on publicly available data on population-based social factors like socioeconomic status, housing, minority status, etc. Prior research has shown that populations with certain socio-demographic characteristics run a higher lifetime risk of being affected by HPV- associated infections and cancers caused by lower vaccination coverage and screening rate.[24,33-35] In the United States, rural residents with poor access to health facilities; racially marginalized populations like the Hispanics, African Americans, and American Indian women; patients who receive vaccines through public funding or those who belong to lower socio-economic strata report lower odds of HPV vaccine series initiation or completion.[24, 33-35]

Vaccination is a key strategy to prevent HPV-related infections and its adverse health outcomes. To promote targeted public health interventions and ensure equitable distribution of health resources identifying and locating vulnerable populations is crucial. Using publicly available census data and a deidentified dataset from Montana's Immunization Information System (ImMTrax), our objective was to examine county-level sociodemographic and healthcare access factors that were associated with higher missed opportunities for HPV vaccination.

7.3 Methods

7.3.1 Data Collection: ImMTrax is a web-based, centralized immunization information system (IIS) that securely stores immunization records for all Montana residents. IIS data are extensively employed in designing and supporting interventions to increase vaccination rates, informing health-related decisions through access to immunization records, facilitating population-based initiatives to curb vaccine-preventable diseases, and surveillance activities.[36] In Montana, healthcare providers voluntarily submit immunization data to ImMTrax. Of all the clinics in Montana that provide immunization

services to children as well as adolescents participate in the federal VFC program, which provides free vaccines for uninsured, underinsured, Medicaid-enrolled and otherwise eligible children and adolescents, and report data to ImMTrax.

Building from results from a prior study which used a limited dataset extracted from ImMTrax,[68] we designed an ecologic study to identify county-level correlates of missed opportunities for HPV vaccination for a cohort of Montana adolescents. Our study sample consisted of adolescents with at least one immunization visit recorded in ImMTrax and who turned 11 years old during 2014-2017. We followed this group up until October 2020 to determine if they ever initiated the HPV vaccine series.

7.3.1.1 Quantification of Missed Opportunities: We considered a clinical encounter or an immunization visit to be a missed opportunity for HPV vaccination if an adolescent between the ages of 11-17 years who was due to receive the HPV vaccine was administered other recommended vaccines (Tdap, meningococcal, and influenza vaccines) but not the HPV vaccine. We analyzed all unique clinical encounters for individuals who turned 11 years old during 2014-2017 and followed them until October 2020 so that we have analyzed a minimum of three years of immunization data for every adolescent in the cohort. During these clinic visits, if an individual received one or more of the other recommended vaccines (Tdap, Meningococcal, or Influenza) but did not receive the HPV vaccine despite being eligible to start the vaccine series, then we classified such visits as missed opportunities for HPV vaccination. We excluded individuals who had initiated the HPV vaccine series before their 11th birthday, had discrepancies in their vaccination records, or who started the HPV vaccine series at any point during the study period from further analyses. We also excluded clinic visits with missing information on the county where the clinic visit occurred.

7.3.1.2 Identification of correlates of missed opportunities: County-level demographic, economic and access-to-care variables were modeled as independent variables. Additional details on the data source, description and estimation methods, and the years during which these data were collected are presented in Table 7.1. In Table 7.1, we present a detailed description of the selected covariates, including the data source, the estimation methods, and the timeframe during which they were collected. County-level sociodemographic variables that were modeled as predictor variables included population density, the percentage of the population considered to be residing in rural areas, the percentage of individuals that are unemployed or lack adequate health insurance, the percentage of the population that identifies as American Indian or Alaska Native, income inequality ratio, the neighborhood deprivation index, proportion of the population within a county that hold a high school diploma and some college education, proportion of population with an internet connection, proportion of children that reside in a single parent household, and families that receive public assistance. Considering the racial and ethnic composition of Montana, I included the county level proportion of American Indian /Alaska Native (AI/AN) population as a predictor variable. American Indian/Alaska Native populations constitute about 6.6% of Montana's population which is largest among all ethnic minorities.[40] Also, Montana counties show a variable distribution of AI/AN populations ranging from 0.1% to 68.1%. Because of this variability, including the county level proportion of American Indian and Alaska Native (AI/AN) population provided us with an opportunity to assess if missed opportunities for HPV vaccination were significantly associated with the county level proportion of American Indian/Alaska Native populations. Selected access-to-care factors included county level per capita rates of primary care physicians, dental providers, registered nurses, advanced practice registered nurses, and licensed practical nurses and mammography screening. Mammography screening was included in the analysis as a proxy measure to assess access and consumption of health resources within a county. In order to

align with the time period pertaining to the immunization records utilized for statistical analyses, we ensured that the data we extracted for the covariates were collected during the same timeframe as mentioned in Table 7.1.

We procured the datasets on these variables primarily from four different sources: the 2022 County Health Rankings Report, United States 2020 Decennial census, the American Community Survey, and occupational licensing data from the Bureau of Labor Statistics.[37-40] Using publicly available datasets, the county-specific neighborhood deprivation index was computed from a principal factor analysis based on certain socio-economic variables like percentage of people within a county holding a Bachelor's degree, percentage of population in managerial occupation, median home value, proportion of households with income greater than $50,000, median household income, and percentage of population receiving an interest/dividend or some type of rental income (data courtesy of Cindy Leary, Center for Population Health Research, University of Montana).[41] Thereafter, depending on the county where the missed opportunity occurred, we linked specific county-level variables data described in Table 7.1 back to individual-level immunization data obtained from the ImMTrax system for statistical modeling.

Table 7.1: **Description of county-level variables with their data sources for model building**

County-level variables	Data Source	Data Collection Timeframe	Measure Methods
Sociodemographic and economic factors			
Population	US Census Bureau, Population Division	2020	Decennial census counts the total number of people residing in the state of Montana
Density per square mile	US Census Bureau, Population Division	2020	Total county population divided by the area of the land mass

Percentage of population that is rural	American Community Survey	2010	The proportion of people residing in geographic areas in a county that are not classified as urbanized areas (>50,000 people) or urban clusters (2,500<county population>50,000) based on the U.S. Census Bureau's urban-rural definitions
Percentage of American Indian/Alaska Native population	Decennial Census	2020	Number of people in a county that identify themselves as American Indians/Alaska Natives divided by the total county population multiplied by 100
Percentage of the uninsured population	Small Area Health Insurance Estimates using the American Community Survey	2019	Percentage of the population under the age of 65 without health insurance obtained by dividing the number of people of currently uninsured in the county under the age of 65 by the number of people in the county under the age 65
Percentage of the unemployed population	United States Bureau of Labor Statistics	2020	The numerator is the total number of people in the civilian labor force, ages 16 and older, who are unemployed but seeking work and the denominator is the total number of people in the civilian labor force, ages 16 and older
Neighborhood Deprivation Index (NDI)	American Community Survey, 5-year estimates	2014-2018	Using principal factor analysis, a county-level NDI estimate based on selected socio-economic factors
Percentage of the population with a high school diploma or equivalent	American Community Survey 5-year estimates	2016-2020	Percentage of adults ages 25 and over with a high school diploma or equivalent
Percentage of the population with some college education but no degree	American Community Survey 5-year estimates	2016-2020	Percentage of adults ages 25-44 with some post-secondary education
Percentage of the population with a broadband internet connection	American Community Survey 5-year estimates	2016-2020	The proportion of individuals that responded "Yes" to at least one of the following types of Internet subscriptions: Broadband such as cable, fiber optic, or

			DSL; a cellular data plan; satellite; a fixed wireless subscription; or other non-dial-up subscription types.
The proportion of children in single-parent households	American Community Survey, 5-year estimates	2016-2020	Numerator is the number of children in family households where the household is headed by a single parent and the denominator is the number of children living in family households in a county.
Income Inequality Ratio	County Health Rankings	2016-2020	The ratio of household income at the 80th percentile to income at the 20th percentile
Percent of households receiving public assistance	American Community Survey, 5-year estimates	2016-2020	Percentage of households that received public assistance income or food stamps/SNAP in the past 12 months
Access-to-care factors			
Per capita primary care providers	County Health Rankings Report	2019	The ratio represents the number of individuals served by one physician in a county, if the population was equally distributed across physicians
Per-capita dental providers	County Health Rankings Report	2019	This ratio represents the population served by one dentist if the entire population of a county was distributed equally across all practicing dentists
Licensed Registered Nurses	Department of Labor and Industry	2020	Number of licensed registered nurses per 10,000 people per county
Advanced Practice Registered Nurses	Department of Labor and Industry	2020	Number of advanced practice registered nurses per 10,000 people per county
Licensed Practical Nurses	Department of Labor and Industry	2020	Number of licensed practical nurses per 10,000 people per county
Rates of mammography screening	County Health Rankings Report	2019	Percentage of female Medicare enrollees ages 65-74 that received an annual mammography screening

7.3.2 Data Analysis: We reported descriptive statistics for all covariates at the county level. The outcome variable of interest was whether or not a clinic visit was a missed opportunity for HPV vaccination. Along with the descriptive statistics, we also estimated the proportion of missed

opportunities summarized across age groups (11-12-year-olds and 13-17-year-olds), gender (males and females), and clinic settings (public health departments, private clinics, IHS/Tribal clinics, rural health centers/FQHCs and other). We used a generalized linear mixed model (GLMM) with a binomial distribution and logit link to determine county-level factors associated with missed opportunities for HPV vaccination. Generalized linear mixed models extend linear mixed models to accommodate noncontinuous outcome variables like binary responses or counts and are especially useful for modeling clustered observations.[42] Since we are expecting observations from the same county to exhibit some level of correlation, generalized linear mixed modeling was determined to be the most appropriate for statistical modeling. In univariate models, we assessed if the association between the odds of experiencing a missed opportunity for HPV vaccination and selected county-level socio-demographic, and access-to-care covariates was significant while adjusting for individuals' age group and gender. We reported the effect sizes by means of adjusted odds ratios (OR) and corresponding 95% confidence intervals (CI).

For multivariate model building, we retained covariates with significant p-values ($p<0.05$) from separate univariate models for the multivariable model. We retained age and gender in the final model irrespective of their significance levels in the univariate model. We expected the effects of county-level variables with significant p-values from the univariate model to differ by individual's age group. So, to test this hypothesis we introduced all two-way interaction terms for age group and all significant covariates in the final model. We modeled the individual's age group and sex as fixed effects and the county in which the clinic visit occurred was modeled as random effect for both univariate and multivariate models. The intraclass correlation coefficients (ICC) of the outcome was estimated to determine the percentage of variability in county-level missed opportunities explained by variabilities in counties versus the combined effects of individual age groups and county-level factors.[47] All the

analyses were performed using SAS V9.4 (Cary, NC) software. We conducted tests for multicollinearity and set the cutoff value for the variance inflation factor at 10. The University of Montana Institutional Review Board approved this study under the exempt category of review.

7.4 Results

There were a total of N= 71,447 clinic visits recorded for 47,622 unique individuals residing in Montana who received any immunization from 2014 to 2017 in the original ImMTrax dataset. Out of these recorded visits, about 53.9% of the visits were missed opportunities to initiate the HPV vaccine series. The county level proportion of missed opportunities ranged from 31.1% to 80.7%. At the end of the follow-up period, about 29,955 (62.9%) adolescents initiated the HPV vaccine series.

Descriptive statistics including the mean, the standard deviation, and the range for predictor variables were estimated at the county level and presented in Table 7.2.

Table 7.2: Descriptive Statistics for sociodemographic, socioeconomic, and access-to-care covariates used in model building (N=56)

Variable	Mean	Standard Deviation	Minimum	Maximum
Population per 2020 census	19296	33,887.7	500	162990
Population Density (number of people per square mile of land area)	8.0	13.4	0.3	61.9
Percentage of population that is rural	75.1	30.8	11.4	100.0
Percentage of American Indian/Alaska Native population	10.9	22.9	0	67.4
Percentage of the uninsured population	12.1	2.9	7.0	20.0
Percentage of the unemployed population	5.3	1.7	3.0	10.0
Neighborhood Deprivation Index (NDI)$^{\beta}$	-0.0001786	1.6	-3.8	3.6

Percentage of the population with a high school diploma or equivalent	32.2	5.3	17.8	41.7
Percentage of the population with some college education but no degree	24.6	3.0	18.1	31.4
Percentage of the population with a broadband internet connection	78.2	5.9	61.7	89.4
The proportion of children in a single-parent household	17.7	9.8	0.0	45.0
Income Inequality Ratio	4.5	1.02	3.0	9.8
Percent of households receiving public assistance	9.7	4.7	0.5	20.4
Per capita primary care providers	1686.7	1046.0	490	6150
Per-capita dental providers	2125.4	1500.3	500	8959
Number of Registered Nurses/10,000 people	116.8	35.8	20	190
Number of Advanced Practice Registered Nurses/10,000 people*	10.7	5.4	1	26
Number of Licensed Practical Nurses/10,000 people	20.3	8.5	8	45
Percentage of women that received a annual mammograms	40.3	7.1	18.0	52.0

β The neighborhood deprivation index (NDI) is a measure of socioeconomic status extracted using the Social Explorer Tool from the American Community Survey conducted between 2014 and 2018. This census tract level index is computed from a principal factor analysis based on the variables % bachelor's degree, % managerial occupation, median home value, % High School education, % interest/dividend/rental income, median household income, and % household income greater than $50,000. A higher NDI score represents more neighborhood deprivation (lower socioeconomic status) [41]

The proportion of missed opportunities for HPV vaccination varied broadly across different counties, with the more rural counties reporting higher missed opportunities as compared to relatively urban areas. In Table 7.3, we have presented the summary statistics for the proportion of missed opportunities for HPV vaccination by adolescents' age groups and gender, and the type of clinic setting where the visit occurred. The mean proportion of missed opportunities for adolescents between the ages of 11-17 years was 61%; with reportedly higher missed opportunities in the 11-12- year-olds when compared to 13-17-year-olds. We found that the mean proportion of missed opportunities was slightly higher among males (62%) than in females (58%). The mean proportion of missed opportunities for

HPV vaccination showed wide variations across different clinic settings. Adolescents were more likely to receive their immunization at a private facility as compared to other clinic settings. Among all clinic settings, immunization visits that occurred in Indian Health Service/Tribal health departments had the lowest proportions of missed opportunities (52%).

Table 7.3: The proportion of missed opportunities for HPV vaccination analyzed across counties by age groups, sex, and clinic settings (n=53*)

	Total clinic visits n (%)	The proportion of clinic visits that were missed opportunities n (%)	Mean ± Standard Deviation	Median (Interquartile Range)	Minimum	Maximum
Age Groups						
Ages 11-12 years	54216 (75.9)	29280 (76.0)	0.61±0.14	0.62 (0.16)	0.29	0.91
Ages 13-17 years	17231 (24.1)	9233 (24.0)	0.57±0.15	0.57 (0.15)	0.00	1.00
Ages 11-17 years	71447(100.0)	38513 (100.0)	0.61±0.12	0.60 (0.15)	0.31	0.92
Sexβ**						
Females	34309 (48.0)	17587 (46.4)	0.58±0.13	0.59 (0.14)	0.26	0.89
Males	36475 (51.1)	20325(53.6)	0.62±0.13	0.62 (0.16)	0.35	0.94
Clinic setting¶**						
Public health departments	17441 (24.1)	11315 (30.3**)**	0.67±0.12	0.67 (0.17)	0.42	0.94
Private clinic	38144 (53.4)	18596 (49.7)	0.60±0.23	0.58 (0.18)	0.00	1.00
Indian Health Service/Tribal Clinic	4330 (6.1)	1633 (4.4)	0.52±0.23	0.51 (0.29)	0.15	1.00
Rural Health Centers/Federally Qualified Health centers	9536 (13.4)	5229 (14.0)	0.58±0.20	0.59 (0.15)	0.00	1.00
Other[α]	754 (1.1)	614 (1.6)	0.92±0.13	1.00 (0.12)	0.55	1.00

***ImMTrax dataset had no record of an immunization visit for Golden Valley, Petroleum, and Judith Basin counties between 2014-2020 ¶** Counties with missing information were excluded from the calculations. **The percentages do not total 100 due to missing clinic setting and sex information. βWe also excluded observations for individuals that reported sex as 'other' or 'unknown' due to fewer responses in each category. αOther types of clinic settings included school-based vaccination centers, urgent care clinics, migrant health centers, hospitals, unknown, and others. Estimates are not adjusted to account for individuals' multiple clinic visits

Using analytic procedures for generalized linear mixed modeling, we fit a univariate model with an alpha level set at 0.05 for each predictor variable while adjusting for the individual's age group and gender and introduced a random intercept for the county where the clinic visit had occurred. In Table 7.4, we present the odds ratios, the corresponding 95% confidence intervals, and p-values for univariate models. We found that increases in population density (p-value=0.02), income inequality ratio (p=0.0017), percentage of children in single-parent households (p=0.0007), percentage of American Indian/ Alaska Native populations (p=0.009) and percentage of households receiving public assistance in a county (p=0.02) were significantly associated with lower odds of experiencing a missed opportunity for HPV vaccination after adjusting for individuals' age and gender. The odds of experiencing a missed opportunity increased by 0.32 times for every 100-unit increase in the county-level population density. Similarly, for every 10-unit increase in the percentages of single-parent households and families receiving public assistance, the odds of experiencing a missed opportunity for initiating the HPV vaccination increased by 0.78 and 0.72 times respectively. Also, for a unit increase in the income inequality ratio, the odds of experiencing a missed opportunity decreased by 19% [aOR=0.81, 95% CI: 0.71-0.92]. Contrary to these findings, adolescents were more likely to experience a missed opportunity if they lived in a county with a higher percentage of census-designated rural areas. [aOR=1.08, 95% CI:1.04-1.13]

The intracluster correlation coefficient (ICC) measures the degree of correlation for observations within the same cluster.[47] We estimated the ICC for an intercept-only model and a full model which contained all the significant variables from the univariate models and the interaction terms for age groups and the significant variables. Based on the ICC for an intercept-only model, we found that 5.2% of the variability in missed opportunities was due to variabilities in counties. The ICC for the full model including the interaction terms for the age group was 0.028; that is 2.8 % of the variability in

missed opportunities was attributed to the differences between the counties. Therefore, about 46.2% of the variability in missed opportunities can be attributed to the combined effects of county-level factors and age groups.

Table 7.4: Logistic regression results for a univariate model adjusted for the individual's age group and gender

Independent Variables	Per Unit Increase	Adjusted Odds Ratio	95% Confidence Intervals	p-value
Density per square mile 2020 census	100	0.32	0.12-0.83	0.02*
Percentage of population that is rural	10	1.08	1.04-1.13	<0.0001*
Percentage of American Indian/Alaska Native population	10	0.93	0.88-0.98	0.009*
Percentage of the uninsured population	10	0.85	0.53-1.37	0.50
Percentage of the unemployed population	10	0.64	0.28-1.48	0.29
Neighborhood Deprivation Index (NDI)	0.1	0.99	0.99-1.00	0.16
Percentage of the population with a high school diploma or equivalent	10	1.20	0.93-1.56	0.16
Percentage of the population with some college education but no degree	10	0.96	0.60-1.54	0.86
Percentage of the population with an internet connection	10	1.08	0.85-1.37	0.54

The proportion of children in a single-parent household	10	0.78	0.68-0.89	0.0007*
Income Inequality Ratio	1	0.81	0.71-0.92	0.0017*
Percent of households receiving public assistance	10	0.72	0.541-0.943	0.02*
Per capita primary care providers	10	1.00	0.99-1.00	0.99
Per-capita Dental Providers	10	1.001	1.000-1.002	0.05
Number of Registered Nurses/10,000 people	10	0.99	0.95-1.03	0.66
Number of Advanced Practice Registered Nurses/10,000 people	10	1.08	0.82-1.42	0.57
Number of Licensed Practical Nurses/10,000 people	10	1.09	0.92-1.28	0.31
% with annual mammograms	10	1.04	0.84-1.28	0.72

*statistically significant p-values ($p<0.05$)

For the final logistic regression model, we included significant variables from the univariate models along with interaction terms for age groups. Table 7.5 displays the results from the multivariable logistic regression analysis. Significance was ascertained by p-values; the cutoff value was set at 0.05. From the final logistic regression model, we found that the two-way interaction terms for age group and density per square mile ($p=0.04$), rurality($p<0.0001$), income inequality ratio ($p=0.009$), percent of households receiving public assistance ($p<0.0001$), and the proportion of children in a single-parent household ($p<0.0001$) were statistically significant while adjusting for other covariates listed in table 6.5. County-level effects of rurality ($p=0.032$), proportion of American Indian/

Alaska Native population (p=0.0098), and income inequality ratio (0.026) were statistically significant after adjusting for age groups, gender, other predictor variables, and interaction terms (Table 7.5). To further assess and quantify the effect of age on the association between missed opportunities for HPV vaccination and county-level variables, we fit separate regression models to report the odds ratio and 95% confidence intervals for age groups and main effects of density, rurality, income inequality ratio, the proportion of children in a single-parent household and the proportion of families receiving public assistance while adjusting for the adolescent's gender as fixed effect and county as random effect.

From the results displayed in Table 7.6, for both age groups, lower income inequality ratio, lower percentage of families receiving public assistance, lower proportion of children living in a single parent household, and lower population density were associated with experiencing higher missed opportunities. The effect sizes were slightly lower among 11-12 year-old age group as compared to 13-17-year olds signaling stronger associations between the outcome variable and predictor variables among 11-12-year-olds. On the contrary, higher proportions of rural population in a county was associated with higher odds of experiencing a missed opportunity for HPV vaccination in both age groups.

Table 7.5: Final multivariate logistic regression model with interaction terms for age group

Predictor Variables	Estimate	Standard Error	F-value	p-value
Intercept	1.0213	0.3606	-	-
Age group (13-17 years)	-0.4398	0.1971	4.98	0.0257*
Gender (Female)	-0.1678	0.01539	118.87	<0.0001
Density per square mile	-0.00189	0.004831	0.49	0.4842
Percentage of population that is rural	0.007864	0.002365	4.60	0.0319*

Percentage of American Indian/Alaska Native population	-0.00628	0.002545	6.66	0.0098*
The proportion of children in a single-parent household	-0.01657	0.008612	0.00	0.9620
Income Inequality Ratio	-0.1990	0.06164	4.96	0.0259*
Percent of households receiving public assistance	0.02368	0.01562	0.02	0.9025
Density per square mile*Age group	-0.00298	0.001239	5.79	0.0161*
Percentage of population that is rural *Age group (13-17 years)	-0.00560	0.000979	32.72	<0.0001*
Percentage of American Indian/Alaska Native population*Age group (13-17 years)	-0.00069	0.001405	0.24	0.6231
The proportion of children in a single-parent household*Age group (13-17 years)	0.03232	0.004695	47.39	<0.0001*
Income Inequality Ratio*Age group (13-17 years)	0.1247	0.04602	7.34	0.0068*
Percent of households receiving public assistance*Age group (13-17 years)	-0.05117	0.007914	41.81	<0.0001*

*****statistically significant p-values ($p<0.05$)

Table 7.6: Logistic regression models fit separately by age groups for significant predictor variables

Predictor Variables	Unit Increase	Age Group (11-12)			Age Group (13-17)		
		Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
Density per square mile	100	0.30	0.10-0.92	0.035*	0.37	0.17-0.82	0.014*
Percentage of population that is rural	10	1.09	1.04-1.14	0.0003*	1.06	1.03-1.10	0.0008*
Income inequality ratio	1	0.77	0.67-0.90	0.0009*	0.87	0.76-0.98	0.04*
The proportion of children in a single-parent household	10	0.76	0.65-0.90	0.0012*	0.81	0.71-0.92	0.0012*
Percent of households receiving public assistance	10	0.70	0.50-0.98	0.03*	0.73	0.57-0.93	0.01*

*****statistically significant p-values ($p<0.05$)

7.5 Discussion

Despite ample evidence on the effectiveness and safety of the HPV vaccine, the uptake among eligible adolescents in Montana has stayed subpar. Previous studies have shown that HPV vaccination disparities exists on a wide range of sociodemographic and socioeconomic characteristics.[44,52-54] In our study, we found a wide variation in the proportions of missed opportunities for HPV vaccination among counties. (Appendix iii, Figures 7.1 and 7.2) Furthermore, ecologic analyses of missed opportunities data revealed that county level effects of density, rurality, income inequality ratio, proportions of families receiving public assistance and children in single parent household, and proportion of American Indian/Alaska Native populations were significantly associated with missed

opportunities for HPV vaccination after adjusting for individual's age group and gender. Our study findings emphasize the need to achieve vaccine equity by improving access and developing programs and policies that target outreach to specific populations that are disproportionately affected by HPV-associated infections.

Even though none of the selected access-to-healthcare factors (per capita primary care physicians, per capita dental providers, number of registered nurses per 10000 people, number of advanced practice registered nurses per 10000 people, number of licensed practical nurses per 10000 people, and percentage of women that received annual mammograms) were significantly associated with experiencing a missed opportunity, past research has shown that accessing healthcare could be particularly challenging in rural areas due to a paucity of health resources.[55] In fact, the majority of Montana counties are designated by the federal government as health professional shortage areas.[56] In our study, we found that as rurality increased, the probability of experiencing a missed opportunity for HPV vaccination also increased. This is similar to what was observed in Indiana and Utah, where researchers found that rurality was significantly associated with experiencing a missed opportunity to receive an HPV vaccine dose.[42,43] In another study from Iowa, researchers reported that teens who sought care from a rural provider were 6% more likely to experience HPV missed opportunities.[52] Higher number missed opportunities for HPV vaccination in rural areas is also reflected in the CDC's NIS-Teen data, where we observe a consistent urban-rural disparity in HPV vaccine uptake.[26] There are several possible explanations for this finding. From previous studies, we know that rural residents have limited HPV vaccine awareness or its role in cancer prevention along with negative community messaging , harbor negative attitudes towards the HPV vaccine, express greater safety concerns, and have greater fatalistic beliefs and cultural views that do not encourage HPV vaccination.[51,44, 57-59] Additionally, providers practicing in rural areas reportedly have less familiarity with HPV vaccine

recommendations and rural parents were less likely to report collaborative parent-provider communication about HPV vaccine.[60] Hesitancy on the part of health care providers to strongly recommend the HPV vaccine might be contributing to higher missed clinical opportunities in rural areas. At an organization level, rural facilities are more likely to face staffing shortages, insufficient vaccine inventory, and time constraints thereby precluding effective vaccine conversations.[61-63] Interventions leveraging patient-provider communication and robust health delivery systems to ensure equitable vaccine distribution and improving public perception regarding the HPV vaccine especially for underserved rural groups, could improve HPV vaccination coverage.

We found that individuals in counties with a higher proportions of the populations that identify themselves as American Indians or Alaska Natives (AI/AN) had lower odds of missed opportunities for HPV vaccine series initiation. In the US, the AI/AN populations experience striking health disparities related to HPV-caused cancer prevalence, rising incidence, and poorer survival among men and women as compared to other racial and ethnic groups.[64] From 2013 to 2017, the incidence of HPV-associated cancers nationally was 1.2 times higher in American Indian and Alaska Native (15.9 per 100,000) than non- Hispanic White (13.7 per 100,000) women.[65] The Indian Health Service (HIS) provides a comprehensive health service delivery system for approximately 2.56 million of the nation's estimated 5.2 million American Indians and Alaska Natives.[66] Past vaccination studies have reported higher rates of HPV vaccine series initiation and completion rates among adolescents who received care at IHS/Tribal clinics as compared to general US populations.[66,67] In fact, adolescents whose mothers identified themselves as AI/ AN were 1.5 times more likely to initiate the HPV vaccine series than adolescents whose mothers identified themselves as Non-Hispanic Whites.[50] In another study, Alaska Native parents demonstrated widespread acceptance of the HPV vaccine and showed willingness to vaccinate their daughters owing to concerns for their health and safety, belief in the efficacy of

vaccines, personal experience with HPV or cancer, and concern for their daughters' susceptibility.[73] Newcomer et al. found that individuals who sought immunizations at an IHS/Tribal Health facility were 38% less likely to not receive the HPV vaccine as compared to those who received their immunization at a private clinic. Researchers in that study theorized that lower missed opportunities at IHS/Tribal clinics could be due to streamlined clinical operations, stronger provider recommendations, or other factors that drive the uptake of HPV vaccine.[68] In a survey of providers working at an IHS/Tribal clinic, Bruegl and colleagues found that that a vast majority of respondents showed willingness to provide both general vaccinations (90%) and the HPV series to both females (98%) and males (88%) and had confidence in the safety and efficacy of the HPV series (90%).[69] In comparison, a statewide survey of Minnesota providers (pediatricians, family medicine physicians, and nurse practitioners) found that only 76% of respondents routinely recommended the HPV vaccine to their female patients ages 11 to 12 years and much fewer, only 46% did so for their male patients.[70] At an organization level, IHS/Tribal clinics support a comprehensive electronic health record system that can be programmed to generate provider prompts whenever an adolescent is due or overdue to receive a vaccine dose, promote use standing orders and reminder-recall for HPV vaccination as reported in a recent study.[67,82] These clinic-level practices have been identified as evidence-based strategies by the Community Preventive Services Taskforce for increasing vaccination coverage.[81] Additionally, provider reminders in EHR systems have shown to increase both HPV initiation and series completion and reduce missed opportunities.[71,72] Multi-level strategies that have been successful in improving HPV vaccination coverage among American Indian and Alaska Native populations could provide valuable insights in to developing interventions for other racial groups that demonstrate high levels of missed opportunities.

A higher income inequality ratio signifies a greater unequal distribution of wealth within a selected subgroup of population.[74] Our study findings reveal that an increase in the income inequality ratio was associated with lower odds of experiencing a missed opportunity for HPV vaccination. These findings could be reflective of the fact that lower rates of vaccine deferrals and refusals are most often documented among families with lower income levels [54,75,76] Studies have also found that providers prioritized HPV vaccine recommendations for certain subpopulations that they perceived to be at a higher risk of HPV-associated infections including adolescents of lower socioeconomic status. Additionally, parents with lower socioeconomic backgrounds were less likely as compared to parents from more socially privileged backgrounds to defer to their providers' advice.[79] In our study we also found that adolescents residing in counties with a higher proportion of families receiving public assistance and single parent households had lower odds of HPV missed opportunities. A plausible underlying explanation for these findings is that counties with higher proportions of families receiving public assistance, families belonging to lower-socioeconomic groups, and single parent households would also have a higher number of adolescents who are eligible to receive subsidized vaccines under the federal vaccine for children (VFC) program.[76, 80] The VFC program provides free vaccines to children who are uninsured, underinsured, Medicaid-eligible, or identify as American Indian or Alaska Native from birth through 18 years of age.[77] Research shows the VFC program has removed financial and logistical barriers, that were historically hindering vaccination for low income children, and therefore likely played a key role in increasing vaccine coverage in this group.[77] Studies of providers with higher participation in the Medicaid or the Vaccines for Children program found that this participation was associated with more positive HPV vaccine recommendation practices.[78,83-85] In fact, in a recently published study, researchers found that providers that received VFC vaccines were more likely than non-VFC participating providers to report "always" recommending HPV vaccine to

patients.[78] Since, a strong vaccine recommendation from a provider is the strongest predictor of parental vaccine acceptance,[79] the odds of experiencing a missed opportunity among teens to receive the HPV vaccine through the VFC program might be reduced. Future studies should seek to explore preventive care seeking attitudes and behaviors among low-income and single-parents and caregivers.

Our study has some limitations. We performed analysis only on Montana's immunization data which limits the generalizability of our study results to other states. The use of county-level data for modeling restricts drawing inferences on an individual level. However, we believe that our study results will have overarching public health implications in helping policymakers identify vulnerable populations and target interventions to increase HPV vaccine uptake. The limitations inherent to using the immunization information system also apply to our study findings. For example, potential misclassification of vaccination status due to missing records or scatter records. Also, the ImMTrax system does not collect information regarding vaccine refusals so we were not able to ascertain the reasons for missed opportunities. Future studies should seek to gain a deeper understanding of barriers to HPV vaccine uptake in each of these counties especially among rural populations that face

7.6 Conclusion

Given the need to effectively allocate sparse health resources to achieve desirable health outcomes, prioritizing Vaccination promotion, outreach, and administration should focus on populations within counties that are highly vulnerable as such regional milieus may have a large impact on health outcomes, and so should play a commensurate role in state-level policy considerations and county-level public health program decisions.

7.6 References

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Chapter 8: Conclusion

Vaccines are one of the greatest public health achievements of the past century but its success is largely dependent on uptake. Often referred to as the 'silent killer' and almost entirely preventable through vaccination, cervical cancer is termed a "disease of inequity of access" by the WHO.[1] Mounting evidence shows that the HPV vaccine is also effective against other anogenital and oropharyngeal cancers.[2-4] However, about 47% of Montana adolescents are not fully vaccinated against HPV and remain vulnerable to HPV-associated cancers.[5] There is a pressing need to implement strategies to address vaccine hesitancy and boost HPV vaccine uptake. Research on vaccine delivery systems has largely focused on pediatricians and family medicine practitioners.[6,7] In rural areas, nurses play a crucial role in implementing programs to improve community health.

Due to their close relationship with the community members, nurses are strategically positioned to positively influence health behaviors and achieve desired health outcomes.[8] From their positioning and recognition in the community and taking advantage of frequent interactions they have daily with users and patients in the different work settings in which they work, nursing professionals can raise public awareness on the importance of vaccination besides participating directly in their administration.[9] Given the growing resistance around vaccines, particularly the HPV vaccine, the development of herd effects and cross immunity through vaccination is likely to be a challenge in regions with lower vaccination coverage. Raising public awareness through education is likely the most crucial role played currently by nurses in the vaccination process.

8.1 Summary of Findings

For my Aim One, I conducted a statewide survey of Montana nurses and medical assistants that worked at a facility that participated in the federal Vaccines for Children program and were involved in adolescent immunization delivery services. The majority of participating nurses strongly agreed or

agreed that the HPV vaccine is important and had confidence in the vaccine's safety. More nurses reported experiencing greater parental vaccine refusal or delay for male versus female patients regardless of age. Study findings identified several promising initiatives to accelerate vaccination in primarily rural states like Montana, including promoting widespread adoption of reminder/recall systems, training nurses in evidence-based techniques to provide strong vaccine recommendations, and leveraging social media to disseminate consistent messages about the HPV vaccine recommendations for both sexes and its role in cancer prevention.

My second research aim was focused on identifying immunization practices at rural public health departments and differentiating factors between public health departments that had higher HPV missed opporutnities and public health departments that had lower HPV missed opportunities. Qualitative analysis of interviews with 21 nurses revealed that greater parental vaccine hesitancy with the HPV vaccine and vaccine communication styles influenced HPV vaccine uptake among adolescents seeking care at rural public health departments. Nurses in higher-performing public health departments presented the HPV vaccine using a presumptive approach in the same way as other adolescent vaccines. However, more nurses in the lower-performing departments presented the HPV vaccine as an 'optional' vaccine using a participatory approach. Nurse participants highlighted the need to engage adolescents through tailored vaccine messaging, create training opportunities for nurses in vaccine conversations, invest in social media campaigns, encourage collaborations with schools and community organizations, and promote HPV vaccination at every patient encounter.

Finally for my third research aim, I conducted an ecologic analysis to identify county-level socioeconomic and access-to-care correlates of missed opportunities for HPV vaccination. Immunization data from ImMTrax, Montana's immunization information system, was used to estimate missed opportunites for HPV vaccination for each Montana county. I used publicly available datasets

like the County Health Rankings, the American Coummunity Survey, and the US Census Bureau for data abstraction on county-level socio-economic and access-to-care predictor variables. After adjusting for age and gender, higher county level proportions of American Indian/Alaska Native population, children in single parent household, families receiving public assistance, the income equality ratio, and population density were significantly associated with experiencing lower odds of missed opportunities for HPV vaccination. Furthermore, increases in the percentage of rurality was significantly associated with higher odds of experiencing a missed opportunity for HPV vaccination while presenting for other adolescent immunizations.

8.2 Public Health Implications and Future Work

Increasing HPV vaccination coverage to 80% is a Healthy People 2030 goal.[10] My dissertation research work has several important public health implications. A crucial way my dissertation contributes to HPV vaccination research is by providing a starting point to investigate different strategies to improve opportunities for HPV vaccination. On a provider level, engaging nurses in HPV vaccine promotion could be facilitated through creating greater training opportunities for nurses in vaccine communication strategies. On a health-system level, supporting implementation of quality improvement projects to increase HPV vaccination rates in public health departments should be prioritized. On a community level, nurses identified a pressing need to increase parental outreach through social media. Strategies identified by Montana nurses closely align with what has been recommended by the National Vaccine Advisory Committee to overcome HPV vaccination barriers in the United States.[11] Future research could expand on our work to evaluate the effectiveness of implementing combined multi-level interventions for increasing HPV vaccination rates particularly in a large, predominately rural state.

8.3 Strengths and Limitations

This dissertation focused on a pressing public health issue of improving HPV vaccination rates in rural and medically underserves areas identified multiple strategies that can improve nurse engagement with promoting HPV vaccination in Montana. Using quantitative and qualitative research methods, we were able to recruit and engage nurses employed at diverse healthcare facilities across the state of Montana. Nurses' responses to the survey questionnaire and interview questions could be subjected to social desirability and recall bias. Additionally, our use of county level data to perform ecologic analysis could lead to ecological fallacy and our study findings should not be used to explain individual-level vaccination characteristics. Finally, because my study population consisted of nurses from Montana, the generalizability of the findings to nurses in other regions may be limited. However, given the urgent need to address persistently low HPV vaccination rates in rural areas of the U.S., this study of nurses and medical assistants in a predominately rural state adds to the limited previous research on engaging healthcare personnel in HPV vaccination promotion efforts in the rural U.S.

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Appendix

i. Data collection instruments

INTRODUCTION

The purpose of this survey is to learn about Montana nurses' experiences with and perceptions of providing vaccines to older children and adolescents ages 9 to 17 years old. The survey is being conducted through a collaboration between the University of Montana Center for Population Health Research and the Montana Department of Public Health and Human Services, with funding from the Centers for Disease Control and Prevention. Your input will help inform public health initiatives and programs.

Your responses are important and will be kept confidential. There is minimal risk of a breach of confidentiality with your survey participation. We will not ask you to provide any identifiable information, and we will take multiple steps to protect the confidentiality of your survey responses, including securely storing survey data. In addition, we will only report survey findings in aggregate. While participating in this survey will provide no direct benefit to you, it will help in identifying areas for improving immunization services for adolescents in Montana.

At the end of the survey, you will be directed to a separate link where you can provide your name and email address to be entered into a drawing. We will be randomly selecting two survey participants to receive a $30 Amazon gift card.

The survey takes approximately 15 minutes to complete. You can skip any questions that you prefer not to answer.

If you have any questions regarding this survey, you may contact Dr. Sophia Newcomer from the University of Montana's Center for Population Health Research at sophia.newcomer@umontana.edu.

By clicking here, you consent to your voluntary participation in the survey.

SECTION 1: NURSE AND CLINIC TYPE

First, we would like to ask you some questions about your role in providing or supporting immunization services in the clinical setting where you work.

1. Do you currently work as a nurse or a medical assistant in Montana?

- Yes
- No

If No, then the survey ends with the message "You have indicated you are not a nurse or medical assistant currently working in Montana and are therefore not eligible to take this survey. Thank you for your time and have a nice day."

2. What type of clinic setting do you work in? If you work across multiple clinics, for this survey, please focus on the clinic where you work most often.
   - Public health clinic, non-tribal
   - Tribal public health clinic
   - Private clinic
   - Other: [text box provided]

   If "Private Clinic" is selected for Q2, then Q2a: Please select your clinic's medical specialty (select all that apply):

   - *Pediatrics*
   - *Family medicine*
   - *Internal medicine*
   - *OB-GYN*
   - *Other: [text box provided]*

3. What is your nursing or medical credential?
   - Medical Assistant (MA)
   - Licensed Practical Nurse (LPN)
   - Registered Nurse (RN)
   - Advanced Practice Registered Nurse (APRN)
   - Other: [text box provided]

   If "Advanced Practice Registered Nurses" is selected for Q3, then Q3a:
   You indicated you are an Advanced Practice Registered Nurse (APRN). Please indicate your role:

- *Certified Nurse Practitioner*
- *Clinical Nurse Specialist*
- *Certified Registered Nurse Anesthetist*
- *Certified Nurse Midwife*
- *Other: [text box provided]*

4. Please tell us about your involvement in immunization services for older children and adolescents. Select all that apply:
   - I administer vaccines to older children or adolescents.
   - I recommend vaccines to parents/guardians or patients.
   - I answer parents' or patients' questions about vaccines.
   - I schedule visits for immunizations.
   - I am involved with ordering vaccines and managing vaccine inventory.
   - I contact parents/guardians to let them know that their child is due or overdue for vaccines.
   - I am involved with immunization services for older children and adolescents in other ways: *[text box provided]*
   - I am not involved with immunization services for older children or adolescents.

   If the last option is selected for Q4, then the survey ends with the message "You have indicated you are not involved with immunizations services for older children or adolescents and are therefore not eligible to take this survey. Thank you for your time and have a nice day."

5. **On average, about how many 9 to 17-year-old patients do you see in a typical week?**
   - 0
   - 1–5
   - 6–10
   - 11–20
   - More than 20
   - Not sure
6. Approximately what percentage of patients to your clinic have public insurance such as Medicaid?

- Less than 25%
- 25%-49%
- 50%-75%
- More than 75%
- Not sure

7. Does your facility participate in the Vaccines for Children (VFC) program?
   - Yes
   - No
   - Not sure

8. Does your facility report vaccinations to ImMTrax?
   - Yes
   - No
   - Not sure

SECTION 2: CLINIC VACCINATION PRACTICES

Next, we would like to ask about your clinic's routine practices for vaccinating older children or adolescents.

9. Which vaccines are routinely offered to older children or adolescent patients in your clinic? Select all that apply.

	Tetanus, diphtheria, and pertussis (Tdap) vaccine	Influenza Vaccine	Meningococcal vaccine	Human papillomavirus (HPV) vaccine
9-10-year old patients				
11-12-year-old patients				
13-14-year-old patients				

15-16-year-old patients				
16-17-year-old patients				

10. Does your clinic have a tracking or reminder/recall system to identify and contact parents/guardians of older children and adolescent patients who are due or overdue for immunizations?

- Yes
- No
- Not sure

If "No" or "Not sure" is selected, then the survey skips to Q.14.

11. What is the method your clinic uses to generate a list to contact parents/guardians about immunizations being due or past due? Select all that apply.

- Reminder/recall list from ImMTrax
- An electronic report from our electronic medical record system
- An electronic report from an administrative or billing system
- A paper-based system
- A tickler file, such as reminder cards that are tracked by nursing or administrative staff
- Other *: [text box provided]*
- Not sure

12. How often are these tracking or reminder/recall lists generated?

- Weekly
- Monthly
- Our clinic generates these lists whenever there is staff capacity to do so.
- Other : [text box provided]
- Not sure

13. How does your clinic contact parents/guardians to let them know that vaccines are due or past due? Select all that apply.

- Phone call
- Email
- Paper letter
- Text message
- Other: *[text box provided]*
- Not sure

14. For the HPV vaccine, two or three doses are needed to complete the series. Does your clinic routinely provide reminders for patients to return for additional HPV vaccine doses?

- Yes
- No
- Not sure

If "No" or "Not sure" is selected, then skip to Q.16

15. How does your clinic remind patients to return for additional HPV vaccine doses? Select all that apply.

- We schedule the follow-up visit before they leave the initial appointment
- We contact them by phone to remind them to return
- We contact them by email to remind them to return
- We contact them by text to remind them to return
- We contact them by letter to remind them to return
- Other: *[text box provided]*
- Not sure

SECTION 3: NURSES EXPERIENCES & PERCEPTIONS

Now we want to ask about your experiences with parents/patients and their knowledge and acceptance of vaccines for older children and adolescents.

16. Have you heard of the MTTeenVax challenge?

- Yes
- No

If "No" is selected, then skip to Q.18

17. Please share your thoughts by answering the following questions about the MT TeenVax Challenge:

	Strongly Agree	Agree	Disagree	Strongly Disagree	Not Sure
Montana TeenVax challenge has increased the awareness about adolescent vaccinations among parents and older children or adolescents in Montana					
Continuing the MT TeenVax challenge will help to boost adolescent immunization rates in Montana					
MT TeenVax challenge has managed to reach the population of parents and older children or adolescents residing in the under-immunized, rural, or underserved areas of Montana					

18. In Montana, a Tdap vaccination is required prior to entering the 7th grade. Which of the following have you observed?

- Most parents are aware that vaccines other than Tdap are recommended to older/children and adolescents.
- Some parents are aware that vaccines other than Tdap are recommended to older/children and adolescents.
- Few parents are aware that vaccines other than Tdap are recommended to older/children and adolescents.

- Not sure.

19. In your experience, what percentage of parents/guardians are aware that the HPV vaccine is recommended in each of the following age groups?

One option can be chosen per row

	Less than 10%	10% - 25%	26% - 50%	More than 50%	Don't know/Not sure
9-10-year-old females					
9-10-year-old-males					
11-12-year-old females					
11-12-year-old males					
13-14-year-old females					
13-14-year-old males					
15-16-year-old females					
15-16-year-old males					

20. In your experience, what percentage of parents and/or patients refuse or defer the HPV vaccine?

One option can be chosen per row

	Less than 10%	10% - 25%	26% - 50%	More than 50%	Don't know/Not sure
9-10-year-old females					
9-10-year-old-males					
11-12-year-old females					

11-12-year-old males					
13-14-year-old females					
13-14-year-old males					
15-16-year-old females					
15-16-year-old males					

21. Based on your experiences as a nurse or medical assistant, are any of the following barriers to older children and adolescents 9-17 years of age receiving the HPV vaccine?

	A major barrier	**Somewhat of a barrier**	**A minor barrier**	**Not at all a barrier**	**Don't know/Not sure**
Misinformation parents receive from the Internet or social media					
Parent concerns about the safety of the HPV vaccine					
Parent concerns that their child will suffer long-term complications from the HPV vaccine					
Parents not thinking that the HPV vaccine is necessary for their sons					
Parents not thinking that the vaccine is necessary for their daughters					

Parent concerns that vaccination may encourage their child to have earlier sexual behavior					
Parent concerns about giving too many vaccines in one visit					
Lack of school entry requirement for an HPV vaccine					
The amount of time it takes to talk about the vaccine with patients					
Parent/patient moral opposition to the HPV vaccine					
Reimbursement issues in some cases					
Medical providers, such as physicians, not recommending the vaccine					
Older children or adolescents delaying regular well-child visits					

22. Based on your experiences as a nurse, are there other barriers to older children and adolescents 9-17 years of age receiving the HPV vaccine?

Open-ended text box provided

SECTION 4: VACCINE ATTITUDES AND BELIEFS

Now, we would like to learn about your thoughts about vaccines for older children and adolescents.

23. Please tell us how much you agree or disagree with the following statements. Please mark only one option per statement.

	Strongly Agree	**Agree**	**Disagree**	**Strongly Disagree**	**Not sure**
It is important that older children or adolescents be vaccinated against HPV before they engage in early physical intimacy, including kissing.					
When I think about discussing the HPV vaccines with parents of 9- to 12-year-old patients, I anticipate having an uncomfortable conversation.					
I think there more resistance to the HPV vaccine compared with the Tdap vaccine because it is not required for school attendance.					
I think there is less resistance from parents and patients to beginning the HPV series at age 13 years or later versus at ages 11-12 years.					
I recommend the HPV vaccine more often for older children or adolescents at higher risk for getting HPV.					
I do not push hard for older children or adolescents to be vaccinated with the HPV vaccine if they are not engaging in risky sexual activity.					
I have confidence in the safety of the HPV vaccine.					

23. In your opinion, how effective do you think the following strategies would be for increasing rates of human papillomavirus vaccination among older children and adolescents?

	Very Effective	Somewhat effective	Neutral	Not effective	Don't know/Not sure
Identification or assignment of an HPV vaccination champion in clinics					
Assembling a quality improvement team for HPV vaccination in clinics					
Requiring HPV vaccination for school attendance					
Training nurses in strategies for effective vaccine conversations					
Training other medical providers, such as physicians, in strategies for effective vaccine conversations					
Having the state public health department use ImMTrax data to contact parents/guardians to let them know their child is due for the HPV vaccine					
Engaging all staff, including clinical and non-clinical staff, in providing to consistent, positive messaging about HPV vaccination to parents and patients					
Partnering with schools or other community organizations to educate parents/guardians about HPV vaccination					

Emphasizing on cancer prevention while recommending HPV vaccine to parents and older children or adolescents					

SECTION 5: FINAL QUESTIONS

Thank you for taking this survey. Your input is important and valuable. We just have a few more questions.

24. Which county do you work in?

Dropdown menu with all Montana counties and a "Prefer not to answer" option

25. For how many years have you worked as a nurse or medical assistant?
    - Less than 2 years
    - 2-6 years
    - 6-10 years
    - 11-15 years
    - 16-20 years
    - More than 20 years
    - Prefer not to answer

26. What is your sex?
    - Female
    - Male
    - Other
    - Prefer not to answer

27. How old are you?
    - Less than 30 years
    - 31- 40 years
    - 41- 50 years

- 51- 60 years
- ≥61 years
- Prefer not to answer

28. Are you of Hispanic, Latino, or Spanish origin?
    - Yes
    - No
    - Prefer not to answer

29. How would you describe yourself?
    - American Indian or Alaska Native
    - Asian
    - Black or African American
    - Native Hawaiian or Other Pacific Islander
    - White
    - Prefer not to answer

SECTION 6: OPEN-ENDED FINAL QUESTION

30. Thank you for participating in this survey. Please use this text box to share any other comments or suggestions regarding immunization practices and strategies for older children and adolescents:
    Text box provided

    _____

ii. Data collection instruments

Semi-structured interview guide

Study: Identifying Nurse- and Clinic-Level Facilitators of HPV Vaccination in Rural Public Health Departments in Montana

Principal Investigator: Sophia Newcomer, Ph.D., MPH, Associate Professor, University of Montana

Research Assistant: Juthika Thaker, MHA, Ph.D. Candidate, University of Montana

Interview Script:

Study Description and Verbal Consent

Hello [participant's name]. Thank you for joining me [on Zoom/in person] today.

Before we get started with the interview, I wanted to share information about this study and see if you have any questions.

My name is Juthika Thaker, and I am a Ph.D. candidate in Public Health at the University of Montana. I am serving as the research assistant on this project. The purpose of this interview is to learn more about clinical workflows, organizational structures, and HPV vaccine practices at your facility. So far, similar studies have been conducted in primary care practices. But, in a largely rural state like Montana, immunization nurses working in public health departments play a crucial role in adolescent immunization services. This study is sponsored by a grant from the CDC and conducted through a collaboration between the University of Montana CPHR [spell] and the Montana DPHHS [spell].

With your permission, we will record this interview and then a study team member will type out or transcribe our discussion. Then, our study team will look for themes across interviews. This information will help in designing evidence-based strategies to improve HPV vaccination rates in Montana, particularly in rural and underserved areas.

To proceed, we will have to record the interview. Do I have your permission to record the interview?

> [If yes] continue.
>
> [If no, end the interview]-Thank you for taking the time to meet with me today. At this point, the interview is concluded, and I have no further questions for you.

We will take steps to protect your confidentiality, including deleting your name from the transcripts of this interview. We will not use your name when we share the results of this study. However, we may use quotes from this interview when we share results. **These quotes will not have your name attached. We will also ensure that there are no elements to the quotes that are identifiable.** Is that, OK?

Your participation is completely voluntary. This means that you do not have to participate in this interview unless you want to. You can skip any questions that you do not prefer to answer. You can end your participation in this interview at any time. The interview should take approximately 45-60 minutes.

Would you be willing to answer some questions on the adolescent immunization practices at your facility?

> [If yes] continue.
>
> [If no]- Thank you for taking the time to meet with me today. At this point, the interview is concluded, and I have no further questions for you.

Thank you for agreeing to participate. I have a list of topics and questions to help guide our discussion. My questions are divided into three broad domains: practice-, provider-, and patient-level barriers to and facilitators of HPV vaccination.

Do you have any questions?

Do I have your permission to begin asking you questions?

Interview Begins Here

Interview Questions

Section 1:

Practice-level Questions:

1. **[Grand Tour Question]:** Could you please tell me about your background and your experience working at this facility?
   Probe: *How long have you been working at the immunization clinic?*

Immunization Workflow at the Facility:

2. **[Grand Tour Question]:** Can you walk me through the process of vaccination at your facility? I am most interested to learn about adolescent vaccinations.
   Probe: *Do you check what other vaccinations are due before or during the visit?*
   Do you recommend vaccinations other than the one they asked for to your patients during the visits?

3. **[Specific/Compare]** How does the administration of the HPV vaccine compare to the administration of other vaccines at your facility?
   Probe: *Do you do anything differently while recommending the vaccine as compared to other adolescent vaccination?*
   How effective have these strategies been in getting parents to accept the HPV vaccine for their children?

4. Please explain to me when and how you bring up the topic of HPV vaccination with parents/patients.
   Probe*:* What are the key points about the vaccine that you address when discussing the HPV vaccine?

   What do you hear most often from patients and their family members about the HPV vaccine?

5. *How do you deal with parents who are vaccine-hesitant and request to delay/refuse the vaccine?*
   Probe: *What resources do you provide them with for information or concerns on HPV-related diseases and the HPV vaccine?*

6. How do you usually conduct HPV vaccine conversations with parents/patients?
   Probe: *Do you recommend the HPV vaccine differently based on the adolescent's gender?*
   Are there any specific populations in your clinic to whom you tailor your messages about the HPV vaccine in a specific way?
   If so, please specify how your messaging differs for these groups.

Barriers to and facilitators of HPV Vaccination:

7. What systems are in place at your clinic to support the initiation of the HPV vaccine series?
   Probe: *Do you face any challenges to their implementation?*
   How effective are these systems?
   In your experience, do you think this system works better for some patients than for others? If so, for whom does it work better/worse?
   How is it better/worse? Why?

8. What systems are in place at your clinic to support the completion of the HPV vaccine series?
   Probe: *How effective are these systems?*
   Do you face any challenges to their implementation?
   In your experience, do you think this system works better for some patients than for others?
   If so, for whom does it work better/worse?
   How is it better/worse? Why?

9. In your practice, what are the things in your opinion that can be done differently to ensure HPV vaccine series initiation and completion?
   Probe: *How feasible would it be to implement these changes and why?*

10. What barriers do your face in recommending or administering the HPV vaccine to your patients?
    Probe: *Do you face any barriers to ordering or stocking the vaccine?*
    How do you think one can overcome these barriers?

Quality Improvement Projects

11. Can you tell me about any quality improvement initiatives or strategies that you have in place for HPV vaccination?
    Probe: What was the motivation behind implementing these QI strategies?
    Have you heard of the AFIX or the IQIP initiatives?

12. *Can you walk me through the process of implementing any new QI initiatives at your facility?*
    [Who initiates it? How is the staff trained on it? What is the staff's response?]
    What are your thoughts about the effectiveness of this/these initiatives in increasing HPV vaccination in your organization?

13. Who takes decisions regarding immunization-related initiatives at your facility?
    Probe: *Do you have an HPV vaccine champion at your facility?*
    Who appointed the HPV Vaccine champion at your facility?
    What is the role of an HPV vaccine champion?
    How would you describe the role of leadership in improving HPV vaccination at your facility?

COVID-19 and its effects on HPV vaccine priority

14. Before the COVID-19 pandemic, to what extent was improving HPV vaccination rates a priority for your organization?
    Probe: *What do you observe at your clinic that tells you that it is a high/low priority?*
    How are you currently prioritizing routine immunizations?

15. *Are there other barriers that limit your public health department's ability to invest more resources in improving HPV vaccination rates?*

16. Has time pressures or staffing shortages impacted your ability to discuss the HPV vaccine with patients and their parents/guardians?
    Probe: *How has it affected?*
    How do you mitigate the issue?

We are almost finished with the first section here. Just a few concluding questions.

17. Please tell me how your facility utilizes ImMTrax, Montana's immunization registry?
    Probe: *Has this helped with streamlining immunization processes? How?*
    What can help with improving the registry?

18. Who do you think are the key stakeholders who should be included in developing strategies to maximize HPV vaccination rates locally?
    Probe: *How can the state health department help in improving HPV vaccination rates in public health departments?*

19. How likely is it that a child over age 12 would come to your clinic without a parent for the second or third dose of the HPV vaccine?
    Probe: *In your opinion, what factors influence whether a child will return to complete the HPV series?*

Thank you for answering my questions. Now, I am going to transition from questions regarding clinic-level factors to your thoughts on HPV-related illnesses and the HPV vaccine.

Section 2:

Provider-level Questions:

1. Could you tell me about your perspectives on HPV vaccination?

2. What do you perceive your role as a provider in ensuring HPV vaccine series completion?
   Probe: *What should it be?*

3. When you think of the health outcomes that an HPV vaccination program is aimed at reducing, in your opinion what are those health outcomes?
   Probe: *How important do you think receipt of all three doses is in ensuring immunity to HPV?*

4. Do you have any concerns with recommending the HPV vaccine to your patients?
   Probe: *Can you tell me more about these concerns?*
   How do you address these concerns? What resources do you prefer?
   Are these concerns more when recommending the vaccine to specific groups of people? If yes, what groups and why?

5. *Do you feel like there is a need for continuing education and training for public health nurses regarding new research on HPV vaccination?*

6. What are your views on the American Academy of Pediatrics recommendation to providers to administer the first dose of the HPV vaccine at 9 years?
   Probe*: Do you think starting early can improve series completion rates?*
   What barriers do you anticipate? How do you think we can overcome these barriers?

7. Are there any resources you use to stay up to date on HPV and HPV vaccine-related information?
   Probe: *How easy or difficult it is to access these resources?*

8. From your perspective, what are the concerns/barriers to HPV vaccine series initiation?
   Probe: *What are the concerns/barriers to HPV vaccine series completion?*
   How can we address these concerns/barriers?

9. In your opinion, what is the most effective strategy for increasing the rate of uptake of the HPV vaccine in your clinic?
   Probe: *What are the challenges to implementation?*
   How can it be addressed?

We are almost finished here. Thank you for answering my questions. I have got just a last few questions focused on parental knowledge, attitudes, and perceptions about the HPV vaccine.

Section 3:

Patient Knowledge and Attitudes:

1. Generally, how knowledgeable do you think patients and their parents are about the HPV vaccine?
   Probe: In your opinion are there any parent/patient characteristics [education, race, socio-economic status] that influence this knowledge?

2. What are the most common questions or concerns that you have received from patients and their parents about the HPV vaccine? Which concern is the most challenging to address in your opinion?
   Probe: *Has this been different with parents of girls versus boys?*
   How do you generally respond to such concerns?

3. From your experiences, what factors encourage parents and patients who have started the HPV vaccine series to complete it?
   Probe: *How can you, as a provider, make it easier for parents/patients to return for additional doses?*

4. What information do you think parents need to know to decide to vaccinate their children against HPV-associated infections?
   Probe: *How do you help parents to navigate HPV vaccine-related decisions?*

Final Thoughts

Is there anything else you would like to let us know about the discussion we had today? Is there anything I didn't ask that would be helpful to us?

Concluding Statement

Thank you for your responses and for taking the time to talk to me today. I do appreciate the time you took to discuss these issues. The interview portion is now concluded.
After the completion of the interviews, we will invite a few nurses to participate in member checking. During member-check, we will share the aggregate study findings with participants to get their feedback to ensure the accuracy of our findings. This would be a short conversation, about 30 minutes. Do I have your permission to contact you in the future regarding this?
The last thing is the gift card incentive. We would like to provide you with a $50 Amazon e-gift card as a thank you for your time. Could you provide me with an email address to that we can send this gift card?

ii. Standards for Reporting Qualitative Research (SRQR)*

http://www.equator-network.org/reporting-guidelines/srqr/

	Page/line no(s).
Title and abstract	
Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	

Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	

Introduction

Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	
Purpose or research question - Purpose of the study and specific objectives or questions	

Methods

Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	
Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	
Context - Setting/site and salient contextual factors; rationale**	
Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	
Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	
Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	
Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	
Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	

Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	
Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	
Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	

Results/findings

Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	
Limitations - Trustworthiness and limitations of findings	

Other

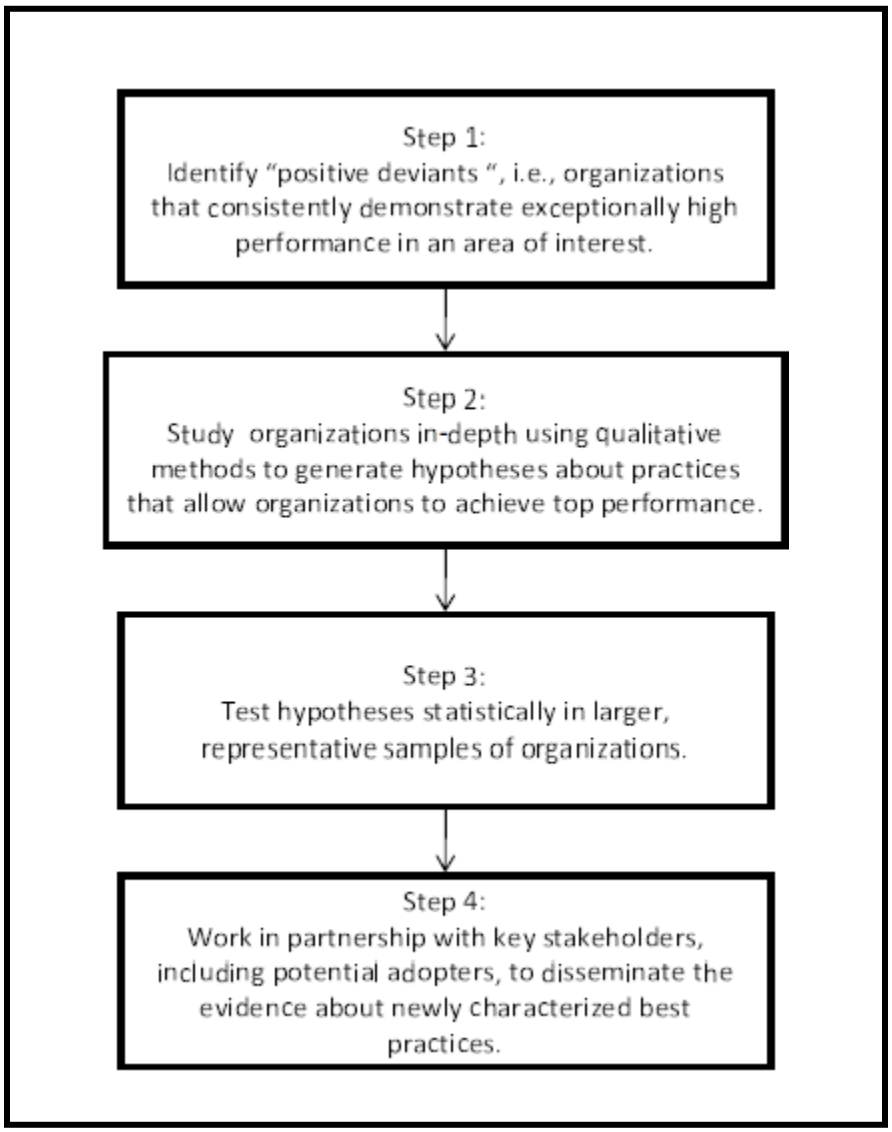
Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	
Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	

*The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

iii.

Figure 5.1: Flowchart summarizing the steps in the positive Deviance Approach



Adapted from Bradley EH, Curry LA, Ramanadhan S, Rowe L, Nembhard IM, Krumholz HM. Research in action: using positive deviance to improve quality of health care. Implement Sci. 2009;4:25.

Figure 6.1: Proportion of immunization visits that were missed opportunities for HPV vaccination among adolescents ages 11-17 years by county for Montana

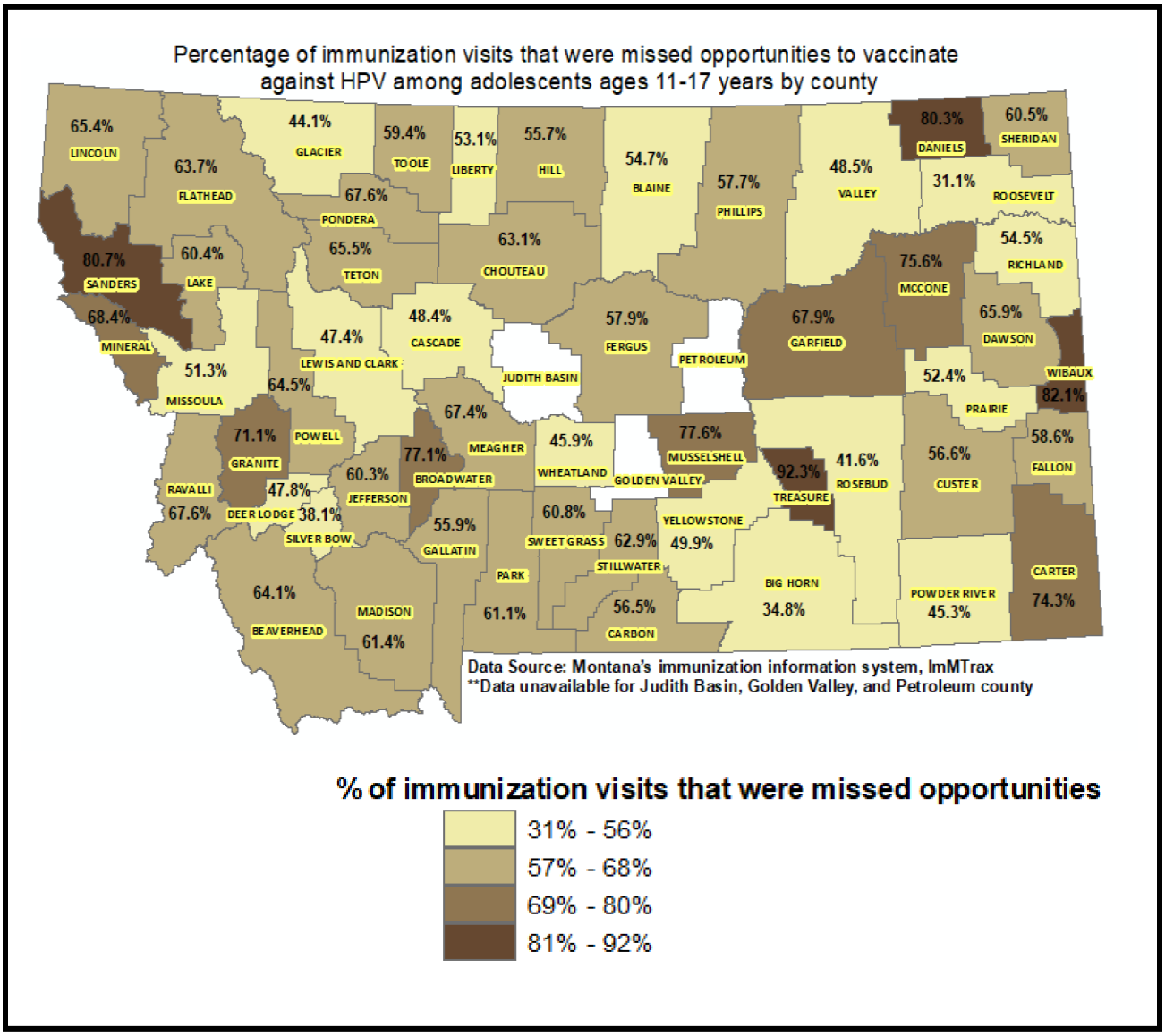
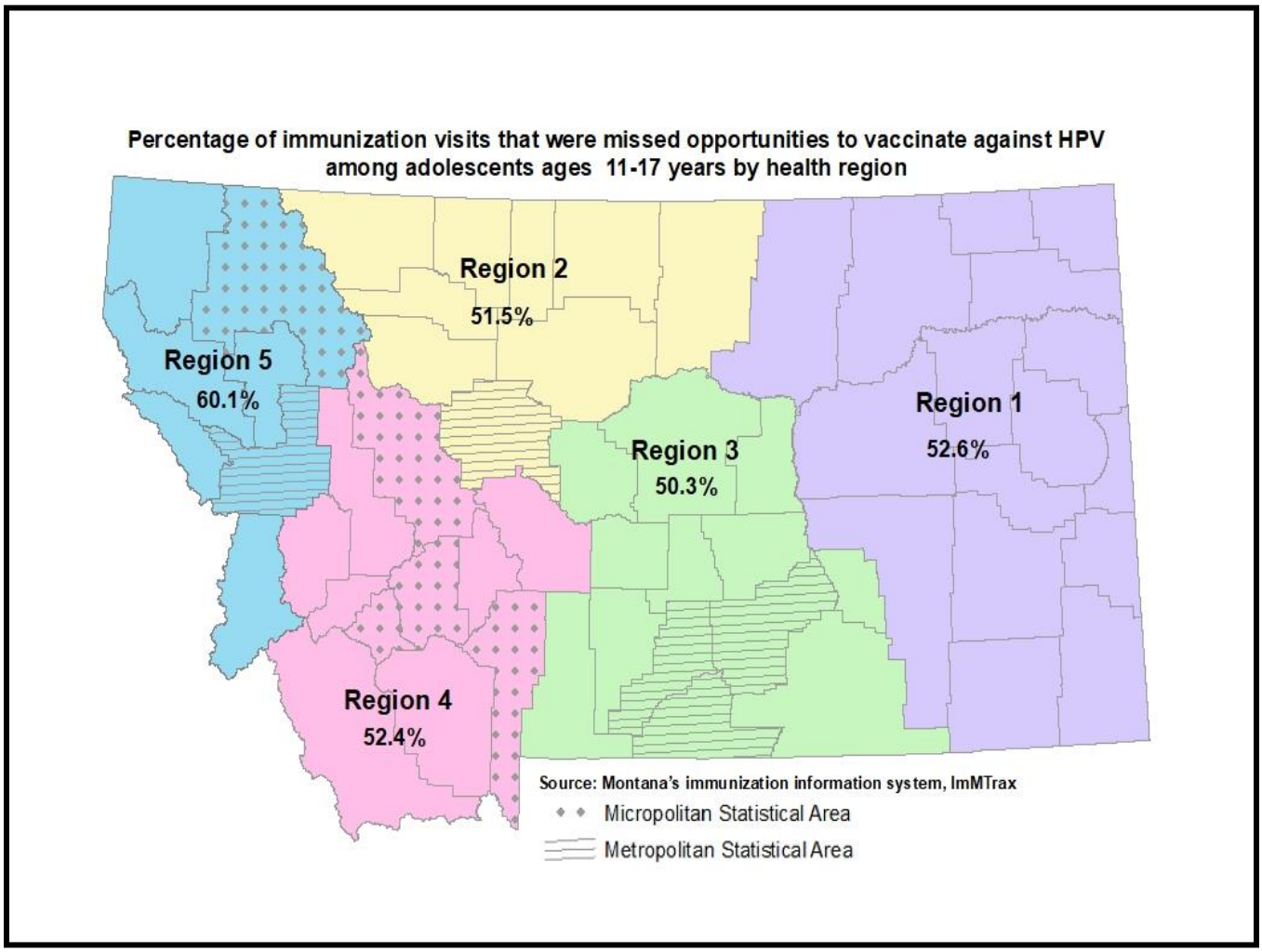


Figure 6.2: Proportion of immunization visits that were missed opportunities for HPV vaccination among adolescents ages 11-17 years by health planning regions for Montana



3.6 References

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