I. Introduction

A. Nature of the research problem

Though recommendations for adolescent immunizations have increased, adolescent immunization rates fall well below childhood rates. Missed opportunities for immunization are well documented, though the conversations that contribute to vaccine hesitancy and refusal are less documented. The process of health communication between health providers, adolescents, and parents that characterizes information transfer in preventive health visits remains a critical but under-explored site for intervention. This project has allowed us to explore vaccine hesitancy in the context of a parent, an adolescent and the team that cares for them. With that information, we have developed a draft training program to increase clinical staff effectiveness in providing adolescent vaccines.

We also explored, as part of a supplement the way in which social media effects public perception of vaccines and examined state specific adolescent vaccination recommendations and rates. As social media create social networks, examining their impact on health behavior is already leading to important new changes, such as disseminating health messages, tracking pandemics, and even prediction of disease outbreaks. If better understood and more widely implemented by medical educators, social media could have an increasingly beneficial impact on the inequalities and disparities surrounding the recommendation and administration of all vaccines. We sought to identify the attitudes and conversations that social media create a platform for and the potential impacts of the shared values of these virtual communities. Knowledge of state specific vaccination recommendations and rates are important for implementing effective local interventions.

B. Purpose, scope, and methods of the investigation

The main purpose of the grant was to explore vaccine hesitancy in the context of parents, adolescent and healthcare providers. We used a mixed-methods approach in our investigation. We had three aims: Specific Aim 1: Establish a baseline rate of delivery of immunizations and other recommended CPS to adolescents through medical record abstraction of office visits with pediatricians, nurses, and family physicians and post-visit surveys of adolescents and parental willingness for vaccines at the practice level for subsequent cluster analysis (Quantitative). Specific Aim 2: Evaluate the knowledge, attitudes, and experiences of pediatricians, family physicians and nurses regarding delivery of immunizations and other CPS to adolescents through the use of in-depth key informant interviews and communication during recorded provider-adolescent/parent interactions during office visits (Qualitative/Quantitative). Specific Aim 3: Using findings from Aims 1 and 2, we will develop and refine an intervention with adolescent, parent, and provider participation to improve communication and decision-making about vaccine delivery, confirming environmental, parental, social, adolescent, and provider factors that act as facilitators and barriers to immunization and health promotion (Qualitative).

In our supplement, there were several objectives. We explored the impact of social media through the analysis of comments to vaccine related stories on the Internet. Then we were to obtain the public health nursing perspective toward our draft simulation intervention to improve immunization delivery to adolescents. Then we explored the state level variation in adolescent immunization attitudes and practices found in the National Immunization Survey.

C. Nature of the findings

This was a mixed-methods multi-modality study. In this study we engaged in large dataset analysis, key informant interviews, focus groups, questionnaires and audio recordings of physician-patient encounters. Most of our findings have fallen into one of several categories: 1) Quantitative adolescent immunization data (national and in three states), reasons for not vaccinating and provider recommendation for vaccination from the National Immunization Survey of Teens (NIS-Teen) 2008-2013; 2) Qualitative data from key informant interviews, focus groups and recorded encounters of parents, adolescents and physicians; 3) Quantitative data from patient encounters that include surveys of parents and adolescents, audits of the medical record for immunizations and preventive services. These methods have been used to explore knowledge, attitudes and behaviors toward immunization or have been related to the immunization status of the patient.
II. Review of the Literature

Human papillomavirus (HPV) is highly infectious, often asymptomatic, sexually transmitted disease that causes a variety of cancers including cervical and oropharyngeal cancer. (D'Souza, Kreimer et al. 2007, Markowitz, Dunne et al. 2007, Gillison, Alemany et al. 2012) Approximately 20 million people in the US are currently infected with the HPV virus; yet the infection is usually asymptomatic. This lack of awareness combined with continued sexual contact with others leads to the widespread nature of the disease.

Completion of the 3-dose HPV series (UTD) in 2014 was 40% in females and 22% in males. (Centers for Disease Control and Prevention 2011, Elam-Evans, Yankey et al. 2014, Stokley, Jeyarajah et al. 2014, Reagan-Steiner, Yankey et al. 2015) In contrast, uptake for the other recently-introduced adolescent vaccines (MCV4 in 2005, Tdap in 2006) (Bilukha and Rosenstein 2005, Broder, Cortese et al. 2006) is much better. (Elam-Evans, Yankey et al. 2014, Stokley, Jeyarajah et al. 2014) In contrast, in 2014, Tdap UTD rate was 88% and MCV was 79%. (Elam-Evans, Yankey et al. 2014, Reagan-Steiner, Yankey et al. 2015)

The consensus of many studies indicate that clinician recommendations are associated with increased receipt of vaccines across ages and vaccines. (Rosenthal, Kottenhahn et al. 1995, Freeman and Freed 1999, Samoff, Dunn et al. 2004, Gnanasekaran, Finkelstein et al. 2006, Winston, Wortley et al. 2006, Nowalk, Lin et al. 2007, Darden and Jacobson 2014) These studies are cross-sectional surveys of patient or parent-reported provider recommendation and are not analysis of actual patient visits. Ylitalo et al. examined the 2009 NIS-Teen survey and found that 60% of female adolescents with provider verified vaccines had received a recommendation for HPV. Those who reported a provider recommendation were almost 5 times more likely to be vaccinated than those who did not. Those findings were consistent across racial/ethnic groups. (Ylitalo, Lee et al. 2013)

Using 2008-2013 NIS-Teen data on MCV, Tdap, and HPV vaccine receipt, our investigative team found that parent-reported clinician recommendation was common and significantly increasing with the magnitude of the increase largest for HPV vaccine, both males and females. (Darden, Thompson et al. 2013) In the 2013 NIS-Teen, we found that parent-reported provider recommendation for HPV vaccine reached 70% for females and 44% for males. (Jacobson, Rogacki et al. 2015) Of note, from 2008 to 2013, parent-reported provider recommendation to females to receive HPV vaccine was greater in all years than for Tdap (57% in 2013) and MCV4 (36% in 2013). (Darden, Thompson et al. 2013, Naifeh, Roberts et al. 2014, Jacobson, Rogacki et al. 2015, Roberts, Naifeh et al. 2015)

Social media is a barometer for public opinion, showing "word-of-mouth" attitudes toward issues, personalities and events. Locating such opinion is particularly important for medical educators as they prepare young clinicians to be ready to face a range of attitudes and beliefs among their patients or, in the case of pediatricians, the parents of the patients as well. The recent report from the Pew Internet Trust on parents and parenting social media comments that 75% of parents turn to social media for information can be perilous. Its reliance on social media for information can be perilous. Its direct marketing can lead to over- or under-consumption of medical technologies or procedures. Social media also offers a new platform for small groups to question medical techniques and potentially spread misinformation, as in anti-vaccination movements. (Keelan, Pavri et al. 2010) One example is the reaction to the (now withdrawn) paper in the Lancet by Andrew Wakefield linking MMR as a possible causal mechanism for autism (Wakefield 1999), resulting in over twenty thousand new cases of measles across Europe. (Centers for Disease Control and Prevention 2011, Mnookin 2011)

Over the past five years, health science researchers have examined how vaccines and vaccination are handled on different social media. In February 2008, researchers collected 146 videos on immunization from YouTube. (Ache and Wallace 2008) finding a range in the quality of information, and an increase in positive video-clips from that found in the earlier study. (Keelan, Pavri-Garcia et al. 2007) Some preliminary attention was paid to viewer comments. A content analysis of 2 months of online news stories about the release of the HPV vaccine found that news stories linked HPV and cervical cancer, but usually without explaining either, and with very little information about safety, side effects, availability and length of protection. (Habel, Liddon et al. 2009)
MySpace blog discourse was captured for a specific day and analyzed for the kinds of arguments made in positive and negative blogs using a 37-item content checklist developed from earlier work. (Keelan, Pavri et al. 2010) An interesting feature was the development of a map of the contiguous US states keyed to density of blog activity and the relationship of such density to positive vs. negative commentary. Texas, California and Florida, for example, had a high percentage of negative comments; New York was strongly positive.

III. Study Design and Methods

A. Study design
There were multiple phases to this project, with qualitative and quantitative designs and methods. Overall these were an observational study design. The patient’s in Aim 1 and 2 were consecutively seen. Focus groups were the staff in the practices that the surveyed patients were from. Key informant interview were with nurses and staff from those same practices. Large dataset analyses involved the National Immunization Survey Teen (NIS-Teen) for various years. In the supplement comments were found by searching for vaccine related articles using common search engines Google, Yahoo and Bing.

B. Population studied
Multiple populations were studied:
- Adolescents 11-17 years of age in the study of hesitancy, recorded visits, focus groups for evaluation of simulation materials and NIS-Teen (adolescents 13-17 years of age)
- Parents of adolescents 11-17 years of age who seen in practices in the study of hesitancy, recorded visits, focus groups for evaluation of simulation materials
- Clinicians (physicians, nurse practitioners, physician assistants) and nurses from network practices in the recorded visits, key informant interviews for attitudes and practices and focus groups for evaluation of simulation materials
- Front office personnel from the network practices in focus groups for attitudes and practices and evaluation of simulation materials

C. Sample selection
- Adolescents 11-17 years of age and their parents in the study of hesitancy and recorded visits were recruited from the waiting rooms of participating practices and the focus groups for evaluation of simulation materials were nominated by the practices and then approached for recruitment
- Clinicians (physicians, nurse practitioners, physician assistants), nurses and front office personnel were from network practices who agreed to participate in this project. These personnel were recruited at the time of consenting for visit recording.

D. Instruments used
- Discussion guides for the focus groups and key informant interviews
- Parent Attitudes about Childhood Vaccines (PACV) modified for use in adolescents
- Chart audit forms for clinical preventive services and adolescent immunizations
- Post-visit Structured Communication Adolescent Guide (SCAG) for the adolescent
- Post-visit survey for parent of adolescent
- Vaccine Decision Making Transcription Tool, coding visit recording transcripts for vaccine recommendation
- Visit Flow Transcription Tool, additional coding visit recording transcripts for initial vaccine recommendation, resistance and persistence/pursuit of recommendation.

E. Statistical techniques employed
Qualitative approaches were used for the focus groups, key informant interviews, and recorded visits, using content analysis, constructivist grounded theory, and discourse analysis. Qualitative coding was done in parallel fashion, categorized and examined for patterns, and summarized by consensus. Quantitative methods included regression techniques (linear and logistic), boot-strapping for some confidence intervals, chi-square and t-tests for bi-variable analysis. Many of our analyses involved cluster-sampling or complex sample designed surveys and so had data requiring the use of statistical techniques for correlated data.
IV. Detailed Findings

Adolescent Immunizations in Office Practice - In examination of parental vaccine hesitancy (see published article #3 below). We modified the vaccine hesitancy survey by Opel, the Parent Attitudes about Childhood Vaccines (PACV), and administered it to approximately 360 adolescents and their parents. We analyzed 363 surveys. At the time of the visit, vaccination coverage was 84% for Tdap, 73% for MCV, and 45% for any dose of HPV. Thirty-nine percent of parents expressed concern about vaccine efficacy and 41% expressed concern about side effects. Forty-five percent of parents disagreed with the statement that “teens can get all of the vaccines that are due at a single visit.” Two individual items were associated with not receiving a dose of HPV vaccine that was due. The overall modified PACV score failed to predict adolescent vaccine uptake at an office visit.

While several individual items were associated with vaccine uptake. The cumulative modified PACV, a general measure of vaccine hesitancy, was not associated with vaccination status despite illuminating parental hesitancy. We need to better understand vaccine-specific concerns for the adolescent population.

In the key informant interviews (KII) from phase two, we found that nurses (n=24) and clinicians (n=36) felt that adolescents and parents were not particularly interested in vaccines. Interestingly, participants in five front office staff focus groups (each with 4-5 participants) reported that parents often left visits with questions that the front office staff were not allowed to address and also the staff personally felt conflicted about HPV vaccine. These KII and focus groups highlight the unmet informational needs in parents and that staff need education to be fully supportive of HPV vaccination efforts.

Also in the second phase of the AVDM study, we examined communication patterns of patients, parents and physicians during immunization discussions. We enrolled adolescent patients 11-17 years of age, who were due for any vaccine, from the same 6 phase-one practices. There were 107 transcripts with usable immunization records available for analysis. Analysis of the transcripts was guided by the principles of conversation analysis and based off of the Four-Habits model. (Maynard and Heritage 2005, Krupat, Frankel et al. 2006) The transcripts were iteratively coded with the content used to best categorize the recommendation that the clinician gave. The final categorization was (Table 1 for examples):

- Expectant provision of vaccines – “Today you will get …”
- Collaborative recommendation – “Today would you like to receive …”
- Directive recommendation (Strong recommendation) – “I recommend that you get …”
- Passive recommendation – “Today you are due for …”
- None – no vaccine communication or recommendation

What we designated as a Directive recommendation is also found in the examples given in CDC materials as the recommendation component of the Strong recommendation and using Opel’s categorization it appears that

<table>
<thead>
<tr>
<th>Table 1: Communication coding examples</th>
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<tbody>
<tr>
<td><strong>Passive recommendation – impersonal recommendation or simple information</strong></td>
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<tr>
<td>“The vaccine that goes more, you know, like it’s a protective vaccine that we do in adolescents, it protects them against Human Papillomavirus. And, but it’s basically a virus which might lead to warts, and it’s also, like, you know, associated with some cancers. So, it’s a prophylactic vaccine that we give most, most of the adolescents in his age.”</td>
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<tr>
<td>“And, finally, well, the Human Papillomavirus, are you familiar with that one?”</td>
</tr>
<tr>
<td><strong>Directive recommendation – a direct and forceful recommendation</strong></td>
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<tr>
<td>“So, I recommend this for all of my kiddos once they’re eleven. HPV vaccine is the only vaccine that we have that actually prevents against cancer.”</td>
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<tr>
<td>“Now, what I think I can speak more confidently to now is it’s safe…So we heartily – I heartily encourage young ladies to get this vaccine, and I would do that.”</td>
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<tr>
<td><strong>Collaborative recommendation – Asking for input into the vaccine decision</strong></td>
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<td>“Okay, If, from what you’ve heard or read, is that something that you’re interested in protecting her with?”</td>
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<tr>
<td>“But since he’s 13 he’s eligible for the HPV vaccination. … You know, would you be interested in doing that as well?”</td>
</tr>
<tr>
<td><strong>Expectant Provision – Assuming agreement to receive the vaccine</strong></td>
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<tr>
<td>“...you need to go ahead and continue with the Gardasil vaccine. …..we’ll go ahead and get the second one now“</td>
</tr>
<tr>
<td>“Well, that’s one of the vaccines that we’ve got to do here today… So good time to get started now. It’s a series of three. He’ll have one today, come back in two months just to see the nurse for the second one, come back four months after that to see the nurse for the third and final one, and be all done.”</td>
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Expectant, Directive and Passive recommendation for vaccines would be categorized as presumptive format while Collaborative provision of vaccines would be categorized as participatory format. (U. S. Department of Health and Human Services and Centers for Disease Control and Prevention 2014)

Examining recommendation by vaccine we found that patients due for HPV vaccine were more likely to receive a Collaborative recommendation than either MCV4 or Tdap (36% vs. 9% and 6%; P<.05). We also found a difference in provider recommendation by patient gender; males were more likely than females to receive Expectant provision for Tdap and MCV (32% vs 17%, Tdap 41% vs 14%; both P<.05). No gender difference in provider recommendation was found with HPV vaccine. There was a difference in vaccine receipt by patient gender for MCV4 and Tdap with males more likely to receive vaccine than females (MCV4 97% vs 75%, Tdap 93% vs 68%; both P<.05).

All vaccines showed an increasing receipt of vaccine when comparing no recommendation to Passive and Directive and then to Collaborative recommendation and to Expectant provision (Figure 1). Our initial hypothesis was that an active, first person recommendation by the clinician, “I want your child to received HPV vaccine” (Directive recommendation), would be the most effective strategy was not supported by these data. Both Expectant provision and a Collaborative recommendation were more effective than either Directive or Passive recommendations. MCV4, Tdap and HPV vaccine recommendation showed a significant trend for receipt of the recommended vaccine going from none to Passive to Directive to Collaborative to Expectant (Chi-square for trend, P<.05). Inspection of Figure 1 suggests that there is a clear grouping in the effectiveness of recommendation types, with none, then Passive and Directive, followed by Collaborative and Expectant. Each vaccines, MCV4, Tdap and HPV, showed a significant trend in receipt of vaccine when categorized in this manner (Chi-square-trend, P<.05 for all vaccines).

**Social Media Exploration** - As part of exploring parent hesitancy toward vaccines and vaccination, the team initiated a study of comments in social media, by collecting public comments responding to stories found via the search engines Yahoo, Google and Bing, and the curated site, Reddit. The collection focused on two days in each of three successive months (July, August and September) in 2013, a year selected because of spikes in public opinion around comments by media and film celebrities including Jenny McCarthy on autism and inoculation and Michael Douglass on oral cancer and HPV. An example from our ongoing study is that of Reddit. Using the terms “vaccine” and “vaccination(s)” we identified subreddits where discussions surrounding these terms took place. We searched Reddit for two consecutive days across three months of time in 2013 (July, August and September) in order to achieve data sufficient for a saturation point for discourse analysis. Using these terms, we captured the URL of each posting in which these terms were discussed as well as the discussion threads themselves, and highlighted and saved the postings to a Word file. We cleaned all postings for subsequent analysis by deleting emoticons, emoji ideograms, robotic messages, photos and advertisements. Using SPSS version 18.0, we generated frequencies on the number of comments per month that appeared on each subreddit using these terms.

Because the text from Reddit was sizeable, with 79,548 words across 17 subreddit groups, each with its own emphasis, we chose to use WMatrix®, a computer-assisted qualitative data analysis (Ayres, Knafl et al. 2008) as a data management tool for an initial content analysis of vaccine(s)/vaccinations and identification of key semantic groupings.
The postings in the various subreddit discussions in the August data set show keen interest in the controversy surrounding vaccines, in whether parents were justified in making the choice not to have a child vaccinated, and in general, decrying non-scientific or anti-vaccinationist platforms. The discussions in September Part 1 are longer, more reflective, and more heavily dependent on reporting findings from other sources. Discussions in September Part 2, arising about the time schools across the US request medical forms including dates of vaccinations, focus on timing for school shots and the pros and cons of the HPV vaccine, currently recommended for middle-schoolers.

V. Discussion and Interpretation of Findings

A. Conclusions to be drawn from findings (The numbers refer to the published references in VI.A.)

Clinician recommendation is very important part of vaccine acceptance (6, 7). Clinician recommendations for adolescent vaccines are increasing over the years with the most frequently recommended vaccine is HPV vaccine in girls (2, 3, 5, 9). The parents of adolescents have a great deal of concerns about vaccines, however the concerns, as we measured them, did not predict vaccine acceptance (4). Vaccine acceptance is lacking for HPV vaccine and there is a great deal of state variability (2, 3, 5). In our examination of interpreted visits (1), we found numerous errors of interpretation with the most common being omission.

Unpublished data but presented in Section IV., we found clear types of recommendation for vaccines. The recommendation was different for HPV vaccine and often HPV vaccine was recommended separately from other vaccines. Interestingly the type also varied by sex of the adolescent for Tdap and MCY but not HPV vaccine. The type of recommendation was associated with receipt of vaccine for all vaccines.

B. Explanation of study limitations

The examinations done have all been qualitative or observational in nature. This makes generalizability for the qualitative studies and causal associations for the observational studies difficult. Involving two states (SC and OK) and for some of the large data set analyses the whole US or three states (MN, SC and OK) provides strength to the associations found they do not necessarily show causation.

C. Comparison with findings of other studies

As opposed to our findings, Opel et al, using conversation analysis (Schegloff 2007) studied vaccine hesitancy in video-recordings of infant encounters found parental resistance to vaccines was lessened and immunization acceptance increased with a presumptive format, in which the provider asserted a position regarding vaccination, as compared to a participatory format, where the parent was asked if they wanted vaccine. (Opel, Robinson et al. 2012, Opel, Heritage et al. 2013, Opel, Mangione-Smith et al. 2015) However, presumptive formats were also associated with a lower parent rated visit experience when compared to participatory formats. (Opel, Mangione-Smith et al. 2015)

We analyzed our audio-recordings Using grounded theory and discourse analysis. (Roberts and Sarangi 2005, Shaw and Bailey 2009). It’s likely that our Expectant, Directive and Passive recommendation styles would be similar to Opel’s presumptive format, while our Collaborative Recommendation would be similar to his participatory format.

D. Possible application of findings to actual MCH health care delivery situations

These findings need to be considered as we consider what are the most appropriate communication strategies for patients.

E. Policy implications

The Centers for Disease Control and Prevention (CDC), health departments and professional organizations are implementing efforts to promote Strong provider recommendation and to eliminate missed opportunities to increase uptake of HPV vaccine. (McInerny 2013, Stokley, Jeyarajah et al. 2014, Centers for Disease Control and Prevention 2015) The CDC’s Strong provider recommendation has three components; 1) information, “HPV vaccine is cancer prevention”, 2) recommendation, “I’m recommending that your child receive the first dose of HPV vaccine” and 3) timing, “today”. (U. S. Department of Health and Human Services and Centers for Disease Control and Prevention 2014) The recommendation component is similar to our Directive recommendation and Opel’s presumptive format. (Opel, Robinson et al. 2012) While this recommended approach makes intuitive sense, there is no empirical literature addressing its effectiveness and our data raise questions about its effectiveness for adolescents.
F. Suggestions for further research

Two recently published studies examining communication strategies highlight the need for explicitly testing patient communication strategies and not relying on expert opinion or even focus group data. Nyan et al, in a 2014 web-based nationally representative survey, tested several recommended communication strategies related to MMR and autism, included were: 1) information about the lack of evidence for MMR and autism, 2) information from the vaccine information statement about the diseases prevented, 3) images of children with the disease, 4) a dramatic narrative about an infant who almost died from measles and, 5) a control group. None of the interventions increased parental intent to vaccinate. Moreover, the information about MMR and autism increased knowledge while decreasing intent to vaccinate. (Nyhan, Reifler et al. 2014) In a study in a 2015 national study, Nyan et al, found that correcting the myth that influenza vaccine caused influenza improved knowledge in a group with concerns about vaccine side effects. This intervention, however, reduced the intent to vaccinate in that group. (Nyhan and Reifler 2015).

These suggest that despite our findings of a superiority of the Expectant and Collaborative recommendation styles these findings should be formally tested rather than relying on observational data, focus groups and expert opinion.

VI. List of products

A. Peer Reviewed Articles


6. Darden PM, Jacobson RM. Impact of a physician recommendation. Human Vaccines & Immunotherapeutics. Published online May 8 2014;10(9). PMID: 24810597


B. Conference Presentations


C. Invited Presentations

Paul M. Darden, MD
1. Adolescent Vaccine Delivery: What the Clinician Says Matters. Pediatric Grand Rounds. Department of Pediatric, Medical University of South Carolina, Charleston, South Carolina, October 23, 2015

2. Effective Delivery of Adolescent Vaccines: It’s all about HPV Vaccine. Pediatric Grand Rounds, Department of Pediatrics, University of Oklahoma, Tulsa, Oklahoma, March 10, 2015.


5. Effective Delivery of Adolescent Vaccines: It’s all about HPV Vaccine. Pediatric Grand Rounds, Department of Pediatrics, Oklahoma University Health Sciences Center, Oklahoma City, Oklahoma, November 12, 2014.

6. The Wonderful World of Adolescent Vaccine Delivery: Why is it so Difficult? Department of Pediatrics, Nationwide Children’s Hospital, Columbus, Ohio, March 20, 2014.

7. Adolescent Immunization: Problems and Possible Solutions. Margaret Q. Jenkins Lecture Pediatric Grand Rounds. Department of Pediatric, Medical University of South Carolina, Charleston, South Carolina, March 14, 2014.


D. Media (Online articles featuring interview quotes by Dr. Paul M. Darden, Dr. Robert Jacobson)


E. Submitted Manuscripts/Manuscripts under Review

None

F. Manuscripts in Progress

1. Darden PM, Davis B, Madden C, Pope C, Roberts JR, Jacobson RM. A little word carries weight in provider-parent-teen vaccine recommendations (submitted once)


4. NIS-Teen (2008-2013) Does clinician recommendation have a different effect by vaccine and has this changed over time?

5. Is there evidence for crowding out of vaccines by other preventive services (or the reverse)?

Detailed references for the background are available on request