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4 Simple and elaborated clinician reminder prompts for HPV vaccination: A randomized clinical  
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6 trial

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42  
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57 and Recommendation Scripts”  
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4 **Abstract**  
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6 **Objective:** To evaluate the effects of simple and elaborated health care provider (HCP) reminder  
7 prompts on human papillomavirus (HPV) vaccine initiation rates.  
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10 **Methods:** Twenty-nine pediatric HCPs serving five pediatric clinics were randomized to one of  
11 three arms: 1) usual practice control; 2) simple reminder prompt; and 3. elaborated reminder  
12 prompt, which included suggested language for recommending the early adolescent platform  
13 vaccines. Prompts were delivered via a computer-based clinical decision support (CDS) system  
14 deployed in the five clinics. Eligible patients were ages 11-13 years, had not received HPV  
15 vaccine, and were due for meningococcal (MenACWY) vaccine and/or the tetanus, diphtheria,  
16 and pertussis booster (Tdap). Receipt of HPV vaccine was determined via automated queries sent  
17 to the Indiana immunization registry. Data were analyzed via logistic regression models, with  
18 generalized estimating equations used to account for the clustering of patients within HCPs.  
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33 **Results:** Ten HCPs in the control group saw 301 patients, 8 HCPs in the simple prompt group  
34 saw 124, and 11 HCPs in the elaborated prompt group saw 223. The elaborated prompt arm had  
35 a higher rate of HPV vaccination (62%) than the control arm (45%): AOR=2.76; 95% CI=1.07-  
36 7.14. The simple prompt arm did not differ significantly from the control arm with respect to  
37 HPV vaccine initiation, which may have been due to the small sample size for this arm.  
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45 MenACWY and Tdap rates did not vary across the three arms.  
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48 **Conclusions:** Results suggest that an elaborated HCP-targeted reminder prompt, with suggested  
49 recommendation language, may improve rates of HPV vaccine initiation.  
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**What's New?**

In this study of pediatric health care providers, we found that an elaborated prompt, which included a suggested recommendation script, resulted in higher first dose administration of HPV vaccine to 11-13 year old patients compared to a usual care condition.

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4 Human papillomavirus (HPV) is the primary cause of nearly all cervical cancers in  
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6 women and many other anogenital and oropharyngeal cancers, as well as genital warts in males  
7  
8 and females.<sup>1</sup> The nine-valent HPV vaccine (9vHPV) has been shown to prevent infection and  
9  
10 disease resulting from the seven HPV types associated with many cancers and the two types  
11  
12 associated with 90% of genital warts (types 6 & 11).<sup>2</sup> Moreover, accumulating evidence  
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14 indicates that the vaccine is quite safe, with few or no severe adverse events tied to vaccination.<sup>3</sup>  
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19 Vaccinating young adolescents prior to sexual debut is important as 9vHPV is a  
20  
21 preventive vaccine and has not been shown to impact infections that have already occurred.  
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23 Moreover, HPV vaccines stimulate a stronger immune response among younger, compared to  
24  
25 older, adolescents.<sup>4</sup> However, the full cost and health benefits of HPV vaccine can only be  
26  
27 realized if the vaccine is widely accepted. HPV vaccination rates in the U.S., while gradually  
28  
29 increasing over time, remain well below the Healthy People 2020 goal of 80% series completion,  
30  
31 and well-below rates for the other early adolescent platform vaccines, meningococcal ACWY  
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33 (MenACWY) and the tetanus, diphtheria, and pertussis booster (Tdap).<sup>5</sup>  
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38 In the U.S., one of the primary parent-identified reasons for vaccinating children against  
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40 HPV was a health care provider's (HCP) recommendation.<sup>6</sup> Similarly, among those who have not  
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42 received HPV vaccine, the lack of HCP recommendation has been identified as a major reason  
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44 for non-vaccination.<sup>7,8</sup> While HCPs generally embrace their important role in recommending  
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46 HPV vaccine, these recommendations may nevertheless be unevenly carried out due to such  
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48 issues as time constraints, perceptions of risk associated with patient age, availability of  
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50 insurance or other coverage, safety and/or efficacy concerns, and the perceived need to discuss  
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52 HPV as a sexually transmitted infection.<sup>9</sup> Vaccine risk communication, in general, is a challenge  
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54 to HCPs.<sup>10</sup> Some providers feel that extensive discussion of risks and benefits of vaccines  
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4 (including sexuality issues related to HPV transmission in particular) might alarm, rather than  
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6 reassure parents, and may take up too much time. Survey research with health care providers  
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8 (HCPs) and audio-recorded conversations between pediatric HCPs and parents of adolescents  
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10 suggest that many struggle with how to effectively recommend HPV vaccine.<sup>11-13</sup>  
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14 One proposed approach to improving HPV vaccination rates and reducing missed  
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16 opportunities for vaccination is implementation of provider reminder prompts delivered via an  
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18 electronic health record (EHR) system. However, prior research on the effects of such prompts  
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20 have shown mixed results.<sup>14-17</sup> The objective of this study was to evaluate the effect of HCP-  
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22 targeted computer-based clinical decision support (CDS) prompts on delivery of adolescent-  
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24 platform vaccines (MenACWY, HPV, Tdap) among adolescents who had not yet received any  
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26 doses of HPV vaccine. In Indiana, there is a large discrepancy between MenACWY and Tdap  
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28 vaccination coverage in adolescents (both around 89% in 2016) and HPV vaccine initiation (54%  
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30 for girls and 37% for boys), highlighting missed opportunities for HPV vaccine administration.  
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32 We evaluated both a simple prompt and an elaborated prompt with suggested recommendation  
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34 language (hereafter referred to as the elaborated prompt condition), with both delivered via an  
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36 EHR system. The inclusion of the elaborated prompt condition represents a unique approach to  
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38 assess CDS prompt effects. We hypothesized a linear increase in HPV vaccination initiation rates  
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40 across the three conditions (representing a reduction in missed opportunities): usual care control,  
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42 simple prompt, and elaborated prompt.  
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## 50 **Methods**

### 51 *Setting*

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53 This study was implemented in five pediatric primary care clinics that are part of  
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55 Eskenazi Health, a large safety net health system serving Marion County, Indiana, which  
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4 includes the city of Indianapolis. The five study clinics are all located in urban Indianapolis and  
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6 serve largely low income, minority children, with 70% of families served on Medicaid. Patients  
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8 are nearly 50% non-Hispanic Black and one third Hispanic. For the 12-month period from March  
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10 2013 to March 2014, there were 3,513 children 11-13 years of age seen at these clinics. The five  
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12 clinics were targeted for this study because all employ the Child Health Improvement through  
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14 Computer Automation (CHICA) CDS system.<sup>17</sup>  
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19 CHICA System. Since 2004 the CHICA system has supported health services research  
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21 related to pediatric care, including screening, counseling, anticipatory guidance, and chronic  
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23 disease diagnosis and management.<sup>18</sup> CHICA is a computer-based CDS system that is unique in  
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25 several respects. These include a tailored user interface, a prioritization scheme that assures the  
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27 HCPs receive the highest priority reminders, and the ability to collect data directly from families  
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29 in the waiting room.<sup>19</sup> CHICA acts as a front end to the EHR system used by Eskenazi. The  
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31 EHR and CHICA communicate using industry standard HL7 communication protocols.<sup>20</sup>  
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36 When a patient checks into a CHICA clinic, CHICA receives a registration message. In  
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38 response CHICA requests a download of the patient's record from the EHR. CHICA applies a  
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40 set of rules to the patient's data to select 20 yes/no questions that are presented to the family via  
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42 electronic tablets. The nurse or medical assistant enters data such as height and weight using the  
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44 same tablet. CHICA applies another set of rules to the patient's record and the data from the  
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46 families to select up to six reminders to deliver to the HCP. Each of these reminders states the  
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48 reason for the reminder and provides up to six check-box responses with which the HCP can  
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50 document his or her response. The HCP's responses are stored as coded data elements, and  
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52 CHICA writes text directly into the EHR documenting the information recorded in the check  
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4 boxes. However, CHICA is not directly linked to order sets and does not lead to a default of the  
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6 vaccines being ordered.  
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9 CHICA has been studied extensively, and several randomized controlled trials have  
10 demonstrated the system's effectiveness in improving adherence to guidelines and quality of  
11 care. For example, CHICA has been applied to parental smoking cessation,<sup>21</sup> preventive  
12 screening,<sup>22</sup> maternal depression screening,<sup>23</sup> ADHD diagnosis,<sup>24</sup> and autism screening.<sup>25</sup>  
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14 Recently we created a link to Indiana's immunization registry, CHIRP, and have developed a  
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16 process for displaying and capturing immunization data through CHICA  
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23 CHICA was installed in its first clinic in 2004. Additional clinics were added over the  
24 next 5 years. Therefore, participating clinics had used CHICA 7 to 12 years at the time of this  
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26 study. Prior to this study CHICA supported vaccination decision making by producing a  
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28 worksheet showing the CDC vaccination grid and indicating which vaccines had been given and  
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30 which were forecast to be due. However, with the exception of seasonal influenza vaccine, there  
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32 were no prompts for other vaccinations prior to this study.  
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### 38 *Participants*

39 All pediatric HCPs (i.e., pediatricians, family physicians, and nurse practitioners) serving  
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41 the five CHICA clinics were included in this study.  
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### 45 *Study Design*

46 To evaluate the effects of two automated HCP reminder interventions on initiation of  
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48 HPV vaccination, we conducted a three-arm randomized control trial. Details of the trial design  
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50 are described in ClinicalTrials.gov (NCT02551887). Briefly, the study used a cluster  
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52 randomization design, where HCPs serving five pediatric clinics in Indianapolis, Indiana, were  
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54 randomized to one of three arms: 1) usual practice control, where vaccination recommendations  
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4 were made by care providers based on their existing methods for determining eligibility; 2)  
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6 computer generated messages reminding providers of MenACWY, HPV, and Tdap vaccination  
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8 eligibility (simple prompt); and 3) computer-generated reminders with a suggested script for  
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10 recommending the three adolescent platform vaccines (elaborated prompt) (see Figure 1 for  
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12 enrollment and allocation diagram). We stratified by clinic site to ensure that all clinics were  
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14 represented in each of the three arms. The content of the simple and elaborated prompts are  
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16 presented in each of the three arms. The content of the simple and elaborated prompts are  
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18 presented in Figure 2. Male and female children 11-13 years of age who had not previously  
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20 received HPV vaccines were eligible for study participation. Children also had to be eligible for  
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22 MenACWY and/or Tdap vaccine. The prompts indicated exactly which of these vaccines was  
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24 due with the HPV vaccine.  
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29 In this study, CHICA identified all children of targeted age then verified their eligibility  
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31 for inclusion by checking their immunization records in CHIRP. Intervention HCPs of eligible  
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33 patients received immunization reminders with or without elaboration at patients' clinical visits.  
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35 During the study period, the HPV prompts (both simple and elaborate) were given the same  
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37 relatively high priority. For example, it was given a higher priority than evaluating ADHD in a  
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39 child with non-specific symptoms of inattention, but a lower priority than a patient experiencing  
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41 food insecurity. Its position (approximately 43rd out of 185) made it very likely that it would  
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43 appear among the six prompts for an eligible patient. On average, HCPs respond to 50% of  
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45 prompts in CHICA.<sup>27</sup> This was consistent in the present study in which 59/124 (48%) of HCPs  
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47 responded to the simple prompt and 112/222 (50%) responded to the elaborate prompt.  
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53 Providers were given no special instruction regarding the HPV prompts. They are used to  
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55 seeing a variety of alerts from CHICA. So there was no particular surprise at seeing a new one.  
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4 The study team meets approximately quarterly with each clinic, and if questions arose, the clinics  
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6 were simply told that CHICA had new reminders about HPV vaccines.  
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9       Receipt of MenACWY, HPV, and Tdap vaccines in all eligible patients was recorded and  
10 confirmed by subsequent queries of CHIRP. If a patient did not receive an HPV vaccine at the  
11 initial visit, that patient was eligible to be enter the study at subsequent visits even if seeing a  
12 HCP in a different arm of the study. The results were analyzed by encounter. So, the patient  
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14 could be counted in both arms on separate occasions. The trial was implemented in 2014-2015.  
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16 The study was approved by a local institutional review board. The requirement for written  
17 informed consent was waived.  
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#### 25 26 *Data Analyses*

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28       Participants' demographic and clinical characteristics were summarized by treatment  
29 group. MenACWY, HPV, and Tdap vaccine uptake rates for the three groups were  
30  
31 comparatively examined. To accommodate the potential correlations in vaccine receipt among  
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33 children seen by the same provider, we performed logistic regression analysis of vaccine uptake  
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35 using generalized estimating equations (GEE). We then repeated the analysis, but controlled for  
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37 the possible effects of patient's sex and race. All analyses were implemented using SAS Version  
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39 9.3 (Cary North Carolina). P values less than 0.05 were considered statistically significant.  
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#### 45 46 **Results**

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48       Thirty-one pediatric HCPs were evaluated for inclusion in this study. Two were deemed  
49 ineligible because they were Adolescent Medicine specialists who saw few children 11-12 years  
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51 of age, leaving 29 HCPs who participated in the study and saw 648 children who met the age  
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53 inclusion criterion of 11-13 years of age and were due for their first HPV vaccine. For 21 of  
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55 these children no information on vaccine administration at the appointment was available,  
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4 meaning the child could not be identified in the immunization registry, leaving 627 eligible  
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6 children. Among the 29 HCPs, 10 were randomized to the control arm and saw 298 patients; 8  
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8 were randomized to the simple reminder group and saw 118 patients; and 11 were randomized to  
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10 the elaborated prompt group and saw 211 patients (see Figure 1). Providers were 67% female  
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12 (n=20), two were nurse practitioners and the remainder were physicians. Patients were 11 (78%),  
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14 12 (16%), and 13 (6%) years of age. Other patient characteristics are summarized in Table 1.  
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19 The HPV vaccination rates for the three intervention groups are presented in Table 1. For  
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21 comparison purposes, the table also includes Tdap and MenACWY vaccination rates. For the  
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23 elaborated prompt group, the HPV vaccination rate (62%) was significantly greater than that in  
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25 the control group (45%; OR=2.74; 95%CI=1.06-7.05;p=0.036). Although the simple prompt  
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27 group appeared to have a higher rate of HPV vaccine administration than the control (59% vs.  
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29 45%) this difference was not statistically significant once adjusted with GEE. Rates of  
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31 MenACWY and Tdap vaccination were not statistically different across the groups. Adjusting  
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33 for patient sex and race/ethnicity, the AOR for the elaborated prompt group remained statistically  
34  
35 significant compared with the control group (AOR=2.76; 95%CI=1.07-7.14; see Table 2). Using  
36  
37 a Cochran-Armatage test, we also found a significant increasing linear trend in HPV vaccination  
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39 rates across the three groups (p<.001). Patient sex also was a significant predictor of first dose  
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41 HPV administration; males had lower odds of receiving vaccine compared with females.  
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48 Post-hoc analyses also were performed to compare the two prompt groups and to evaluate  
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50 the combined elaborated and simple prompt groups to the control. Although nearly statistically  
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52 significant, the elaborated prompt group was not different from the simple prompt group  
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54 (AOR=2.49; 95%CI=.98-6.35; p=.06). Furthermore, a combined analysis of any prompt  
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4 compared to the control indicated no significant difference between the two groups (AOR=1.83;  
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6 95% CI=.86-3.90).  
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## 9 **Discussion**

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11 In this randomized trial, we tested the introduction of a simple prompt, a traditional form  
12 of clinical decision support facilitated by an electronic health record system, to remind HCPs  
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14 about vaccine eligibility, and an elaborated prompt, a form of clinical decision support that  
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16 included a suggested script to use when recommending vaccines to patients. Results from the  
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18 trial indicate that while the simple prompt did not have an effect, the elaborated prompt  
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20 significantly improved the rate of first dose administration of the HPV vaccine when compared  
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22 to a control group. All three arms of the study had similar vaccine administration rates for Tdap  
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24 and MenACWY, underscoring the effect of the elaborated prompt on the HPV vaccine. The  
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26 results are further noteworthy as they occurred in a population of underrepresented groups where  
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28 neither race nor ethnicity was a determinant in the vaccine administration rate.  
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36 The results from this trial contribute to a growing body of literature assessing the impact  
37 of decision support delivered via information and communications technologies on vaccine  
38 uptake. Recent reviews of the evidence on CDS technologies to remind providers about vaccine  
39 eligibility trend towards the positive but remain mixed.<sup>26,27</sup> Although a pre-post study found no  
40 effect of reminder prompts,<sup>17</sup> a retrospective cohort study observed higher HPV vaccine uptake  
41 for female patients attending clinics that used electronic prompts compared with those who  
42 attending clinics that did not use prompts.<sup>15</sup> Similarly, a multi-component HCP-focused  
43 intervention that included EHR-based alerts increased first dose administration<sup>14</sup> and reduced  
44 missed opportunities for HPV vaccination.<sup>30</sup> However, a cluster randomized trial that evaluated a  
45 simple reminder prompt found no difference in uptake in a diverse population of adolescents.<sup>16</sup>  
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4 These reviews and research studies, as well as other reviews of information and communications  
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6 technology interventions to improve vaccine uptake,<sup>31,32</sup> suggest that reminders to providers may  
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8 work best in combination with interventions that remind or educate patients, as the decision to  
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10 vaccinate is one often made in the context of a patient-provider relationship. In this trial, we  
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12 observed a statistically significant 17% higher rate of HPV vaccine uptake in the elaborated  
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14 prompt group and a non-significant but encouraging 14% higher rate in the simple prompt group.  
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16 Given that the simple prompt group had the smallest sample size, it is possible that the lack of  
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18 significance was due to inadequate power. Further, the elaborated prompt group did not have  
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20 significantly higher HPV vaccination rates than the simple prompt group. Therefore, we cannot  
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22 conclusively state that the elaborated prompt was better than the simple prompt intervention or  
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24 that the simple prompt was ineffective. However, this trial adds evidence that provider-targeted  
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26 CDS prompts can be effective at increasing vaccine uptake in diverse patient populations.  
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28 Interestingly, interviews conducted with the HCPs after completion of the study indicated that  
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30 most recalled seeing the prompts, but few believed that the prompts influenced their behavior,  
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32 despite evidence to the contrary.<sup>33</sup> Additionally, HPV vaccination rates did not rise to the same  
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34 level as Tdap and MenACWY, suggesting that a combination strategy involving patient  
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36 education as well as reminders sent directly to patients, strategies identified in the systematic  
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38 reviews, might have further increased vaccine uptake in our population.  
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48 An important limitation in this study as well as all studies involving provider-targeted  
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50 CDS interventions<sup>31</sup> is that CDS only has the potential to improve vaccination rates for those  
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52 who come to clinics. This limitation suggests that future work should include study of more  
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54 complex CDS interventions that, in parallel, provide reminders to HCPs as well as patients and  
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56 families. Another limitation is the unequal distribution of HCPs across conditions, a problem that  
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4 can occur when randomizing small numbers of participants. The clinics represented in this study  
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6 were all located in one urban area and all utilized the CHICA CDS system, potentially limiting  
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8 generalizability of the findings to clinics in other locations and clinics that do not use the CHICA  
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10 system. Furthermore, we did not have baseline HCP vaccination rates and it is possible that more  
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12 effective vaccinators happened to be randomized to the elaborated prompt group, particularly  
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14 given the relatively small number of providers. However, we did not find that Tdap or  
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16 MenACWY vaccination rates varied across the three groups, suggesting that the HCPs in the  
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18 elaborated prompt group were not, in general, more effective vaccinators than those in the other  
19  
20 two conditions. Also, we did not stratify on the basis of number of patients 11-13 typically seen  
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22 by the HCPs. As a result, the simple prompt group ended up with fewer patients represented than  
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24 the other two arms. Finally, data were collected several years ago, in 2013-2014 and it is possible  
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26 that changes in practice since that time might make the study interventions less or more effective.  
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28 Despite these limitations, the results of this study point in a promising direction, showing that an  
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30 elaborated EHR prompt, which included suggested language for recommending adolescent  
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32 vaccines, significantly enhanced administration of the first dose of HPV vaccine compared to the  
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34 usual care control group. A wider evaluation of this kind of elaborated prompt using established  
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36 EHR systems would be a valuable next step.  
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Table 1. Sample characteristics across intervention groups

	Intervention Condition		
	Control	Prompt	Elaborated Prompt
HCPs	10	8	11
Patients	301	124	223
%Female	43%	45%	47%
Race/Ethnicity			
Non-Hispanic Black	49.8%	70.2%	38.1%
Non-Hispanic White	12.0%	7.3%	13.5%
Hispanic	17.3%	5.6%	30.0%
Other/Unknown	20.9%	16.9%	18.4%
HPV – 1 <sup>st</sup> Dose	45%	59%	62%
Tdap	82%	83%	83%
MenACWY	81%	81%	83%
HPV – 2 <sup>nd</sup> Dose (of those eligible)	80%	81%	80%

Table 2. Adjusted multivariable logistic regression with GEE predicting HPV vaccine initiation

	AOR	95% CI	P-value
<b>Intervention</b>			
Control	Reference		
Simple Prompt	1.11	0.50-2.48	0.800
Elaborated Prompt	2.76	1.07-7.14	0.036
<b>Sex</b>			
Female	Reference		
Male	0.68	0.55-0.83	0.001
<b>Race</b>			
Non-Hispanic Black	Reference		
Non-Hispanic White	0.66	0.35-1.22	0.183
Hispanic	0.89	0.47-1.68	0.717
Other	0.87	0.47-1.62	0.663



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Figure 1. Enrollment and group allocation

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Figure 2. Content of simple and elaborated prompts. Prompts showed which of the vaccines (MenACWY and/or DTaP) was due with the HPV.

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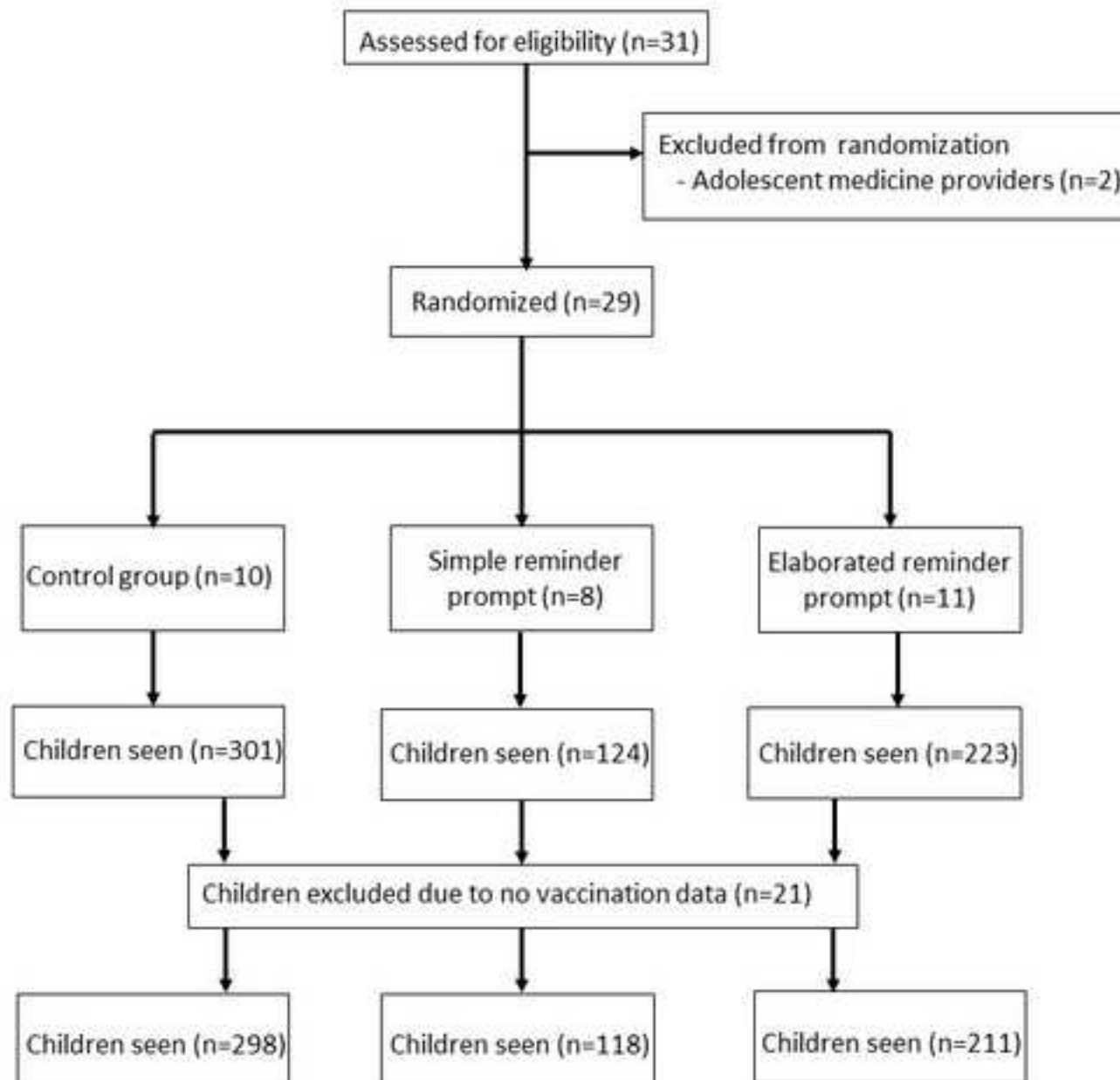
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Figure(s)

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### Simple Prompt:

Vaccines to consider today (check shots given):

- |  |   |
|--|---|
| <input type="checkbox"/> Meningococcal | <input type="checkbox"/>                                    |
| <input type="checkbox"/> HPV ----->    | <input type="checkbox"/> Scheduled follow-up for next dose. |
| <input type="checkbox"/> Tdap          | <input type="checkbox"/>                                    |

### Elaborated Prompt:

Three vaccines are recommended for <first name>, meningococcal to prevent Meningitis, HPV to prevent cancer, and Tdap to prevent tetanus. All three are Recommended at this age (check shots given):

- |  |   |
|--|---|
| <input type="checkbox"/> Meningococcal | <input type="checkbox"/>                                    |
| <input type="checkbox"/> HPV ----->    | <input type="checkbox"/> Scheduled follow-up for next dose. |
| <input type="checkbox"/> Tdap          | <input type="checkbox"/>                                    |