Effect of Decision Support on Missed Opportunities for Human Papillomavirus Vaccination

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Background: Missed opportunities for human papilloma virus (HPV) vaccination are common, presenting a barrier to achieving widespread vaccine coverage and preventing infection.

Purpose: To compare the impact of clinician- versus family-focused decision support, none, or both on captured opportunities for HPV vaccination.

Design: Twelve-month cluster randomized controlled trial conducted in 2010–2011.

Setting/participants: Adolescent girls aged 11–17 years due for HPV Dose 1, 2, or 3 receiving care at primary care practices.

Intervention: Twenty-two primary care practices were cluster randomized to receive a three-part clinician-focused intervention (educational sessions, electronic health record–based alerts, and performance feedback) or none. Within each practice, girls were randomized at the patient level to receive family-focused, automated, educational phone calls or none. Randomization resulted in four groups: clinician-focused, family-focused, combined, or no intervention.

Main outcome measures: Standardized proportions of captured opportunities (due vaccine received at clinician visit) were calculated among girls in each study arm. Analyses were conducted in 2013.

Results: Among 17,016 adolescent girls and their 32,472 visits (14,247 preventive, 18,225 acute), more HPV opportunities were captured at preventive than acute visits (36% vs 4%, $p < 0.001$). At preventive visits, the clinician intervention increased captured opportunities by 9 percentage points for HPV-1 and 6 percentage points for HPV-3 ($p \leq 0.01$), but not HPV-2. At acute visits, the clinician and combined interventions significantly improved captured opportunities for all three doses ($p \leq 0.01$). The family intervention was similar to none. Results differed by practice setting; at preventive visits, the clinician intervention was more effective for HPV-1 in suburban than urban settings, whereas at acute visits, the clinician intervention was more effective for all doses at urban practices.

Conclusions: Clinician-focused decision support is a more effective strategy than family-focused to prevent missed HPV vaccination opportunities. Given the persistence of missed opportunities even in intervention groups, complementary strategies are needed. This study is registered at clinicaltrials.gov NCT01159093.

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Introduction

Human papillomavirus (HPV) is a common sexually transmitted infection that can cause cervical cancer, genital warts, and other cancers. Annually, approximately 14 million people are newly infected in the U.S.[1] Twenty-six thousand new cases of HPV-related cancer are identified each year,[2] and approximately $4 billion are spent annually to manage all the consequences of HPV infection.[3] A three-dose HPV vaccine series was licensed in 2006 for use in female patients aged 9–26 years,[4] for male patients in 2009,[5] and is now widely available. Despite recommendation by the Advisory Committee on Immunization Practices (ACIP), HPV vaccine coverage rates remain lower than other adolescent immunizations.[6]

Missed opportunities present a substantial barrier to achieving widespread HPV coverage.[7–10] A missed opportunity is defined as any time a vaccine-eligible patient presents for care but remains unvaccinated.[10] Previous research[10] found that 64% of adolescent girls had a missed opportunity for HPV vaccine Dose 1 (HPV-1) at their 11–12-year preventive care visits compared to 45% for the tetanus–diphtheria–pertussis booster (Tdap) and 52% for the meningococcal conjugate vaccine (MCV). A recent CDC report[11] found that from 2007 to 2012, the proportion of girls who missed opportunities for HPV vaccination increased from 21% to 84%. Reflecting the importance of preventing missed opportunities, the report[11] found that if all missed opportunities had been eliminated, more than 90% of girls would have received at least one dose of the HPV vaccine.

Prior work has documented that missed opportunities result from primary care providers failing to strongly recommend the vaccine at visits,[9,12,13] parents refusing or delaying vaccination,[13,14] and adolescents presenting for acute visits instead of preventive care.[15–18] Examining data at the visit level provides unique insights about how to motivate effective communication around HPV vaccine receipt, including supporting strong clinician recommendations and mitigating parental resistance in the context of both acute and preventive care.

Health information technology in clinical care provides a promising approach to facilitate communication at the visit level and reduce missed immunization opportunities. Electronic health record (EHR)–based clinical decision support for pediatric vaccination has proven effective in some, but not all, studies.[19–21] Additionally, reminder phone calls to families may help reduce missed opportunities by communicating the benefits of vaccination and reminding families to schedule appointments. Such calls have been used previously to improve vaccination rates,[22–24] but previous work has not focused on their effectiveness in combination with EHR-based decision support.

To address the knowledge gap regarding the relative benefits of decision support to families, clinicians, or both to reduce missed opportunities, the present research team conducted a new analysis of data from a large clinical trial, which evaluated a two-pronged decision support intervention that targeted both providers and patients to increase HPV vaccine receipt. The original study, which focused on a patient-level analysis of vaccination rates, found that clinician-focused decision support was more effective in improving girls' rates of vaccination for HPV-1, and family-focused decision support was more effective in improving vaccination rates for the second and third doses.[25] This article extends that prior work by examining the effect of clinician- and family-focused decision support, alone and in combination, on missed opportunities for vaccination at the visit level in order to evaluate the effect of decision support in the context of primary care visits.

Methods

Setting

This study was conducted within the Children's Hospital of Philadelphia (CHOP) Pediatric Research Consortium (PeRC), a hospital-owned primary care practice–based research network including 31 practices and 200,000 children in two states.[26] Four urban, resident teaching practices and 18 primarily suburban practices not involved in resident teaching participated. All practices used the same EHR (Epic Systems, Inc., Verona WI).

Study Design and Patient Population

The current study is a secondary analysis of a previously published trial.[25] Twenty-two participating primary care practices were first cluster-randomized at the practice level into two groups of 11 practices. Each group received either a three-part clinical decision support intervention including EHR-based clinician-focused vaccine alerts, education, and audit and feedback or no practice-level intervention (Figure 1). Patients were then randomized within each practice to receive automated educational reminder calls or no patient-level intervention. This resulted in four study arms: combined intervention, clinician decision support only, family decision support only, and neither. The 1-year intervention began on May 10, 2010.

The overall clinical trial population included all girls aged 11–17 years due for at least one dose of the HPV vaccine during the study period. This study only included girls because, although the HPV vaccine had been licensed for use in both boys and girls at the time of the study, ACIP recommended the vaccine for girls, but it was optional for boys.[4,27] The current analysis included only girls who had at least one acute or preventive visit with a pediatrician or nurse practitioner during the study period; some girls randomized in the overall trial[25] never had an office visit with a clinician (Figure 1).

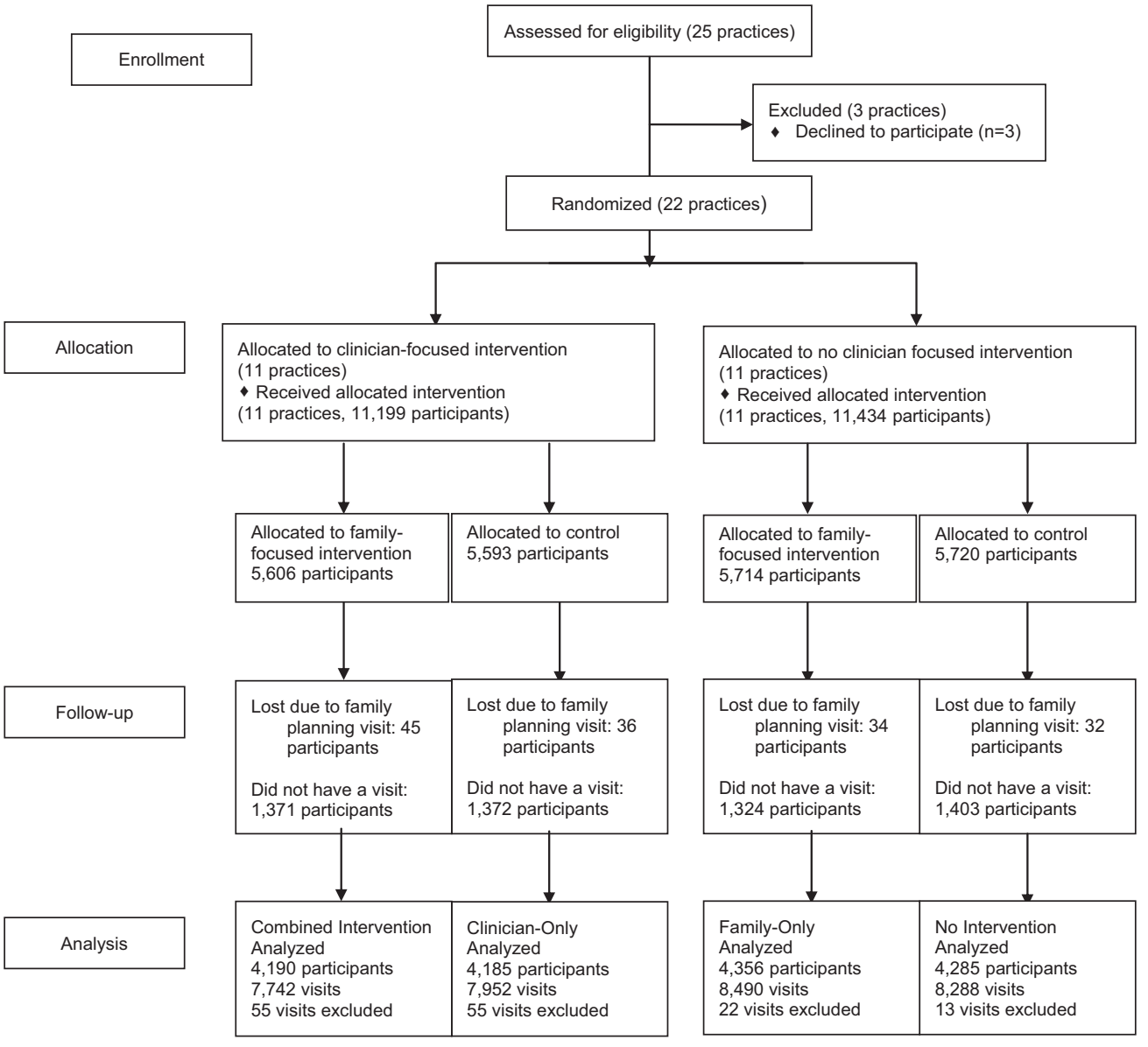

Figure 1. Randomization of study subjects.

Note: Girls were randomized as they became eligible during the study period. Adolescents vaccinated at family planning visits were excluded to protect confidentiality. Only girls who had at least one acute or preventive visit during the study period were included in the analysis. Nurse or medical assistant only visits were excluded.

Interventions

The clinician-focused intervention consisted of three components: (1) EHR-based vaccine alerts for any due vaccines programmed to appear prominently whenever any patient encounter was opened within the EHR; (2) a 1-hour educational presentation about the HPV vaccine; and (3) three quarterly performance feedback reports including individual, practice, and network rates of captured immunization opportunities for HPV, Tdap, and MCV at office visits.[25] Control practices received none of these interventions.

In the family-focused intervention, an outside vendor (Televox Software, Inc., Mobile AL) generated automated phone calls based on an EHR-generated roster. Intervention subjects with study vaccines due (HPV, Tdap, or MCV) received reminder phone calls to their primary phone number on record in the EHR to notify them of any due vaccines, refer them to an educational website, and remind them of upcoming preventive visits (Appendix Table 1). The study provided no reminder calls to girls in the control group.

Randomization

For the clinician-focused intervention, study practices were stratified into urban versus suburban practices and further by baseline rates of HPV-1 vaccination and then randomized.[25] The contrast between urban and suburban practices was considered pre-randomization because of differences in vaccination patterns between these settings. For the family-focused intervention, subjects

were randomized within each of two age categories (11–13 or 14–17 years) within the 22 practices using randomly permuted blocks with unequal block sizes to ensure blinded allocation and balanced assignment within practices. Patient-level randomization was stratified by age, as intention to vaccinate and actual vaccination rates are higher among older adolescents.[6,13,28,29]

Measures

The primary outcome of the present study was the proportion of captured immunization opportunities for HPV vaccination at the visit level. A "captured opportunity" was defined as an eligible visit at which the HPV vaccine was received. Eligible visits included completed preventive and acute care visits at which study participants were due for any dose of the HPV vaccine and seen by a physician, nurse practitioner, resident, or fellow during the 1-year study period. Visits with nurses or medical assistants only were excluded. Outcome data were collected from the EHR.

Covariates controlled for demographic and clinical characteristics that might potentially influence the effect of the interventions on vaccination and were collected from the EHR (Table 1).

Statistical Analysis

The proportion of visits at which each dose of the HPV vaccine was received was calculated for each of the four study arms, overall and stratified by preventive versus acute visit type; this was done separately for all HPV doses. In order to examine potential differences in subgroups of girls, proportions of captured opportunities stratified by age (11–13 years versus 14–17 years) and by urban versus suburban practice setting were calculated.

Multivariable logistic regression with variances adjusted for the cluster-randomized design (clustering by practices)[30] was implemented to compare captured opportunities among study arms, adjusting for covariates (Table 1). The analysis did not account for multiple visits separately by individual girls with a single clinician because marginal models for binary outcomes with robust variance estimates that allow for clustering at the level of randomization are standard methods for cluster randomized designs, and also produce acceptable variance estimates, even when clustering occurs at multiple levels (provider and patient).[31–33]

Comparisons from logistic regression were transformed into standardized proportions using marginal standardization.[34] These standardized proportions were interpreted as the expected proportion that would be vaccinated if the entire sample were alternatively subjected to each intervention arm or monitored as a control group, controlling for covariates.[35]

As a secondary analysis, standardized proportions were calculated separately for 11–13- and 14–17-year-olds and for urban and suburban practices. Models including an interaction term between study arm and age group were implemented; however, a formal test of interaction based on practice setting was not explored because practice was the unit of clinician randomization and the study had only four urban practices. However, given the differences observed between urban and suburban settings, separate results are presented for these groups. In an additional analysis, proportions of captured immunization opportunities were calculated only at visits where at least one other adolescent vaccine (Tdap, MCV, or varicella) was received.

Analyses were conducted in 2013 and performed using Stata, version 12.1, using the "logistic" procedure with the "vce" option. The "margins" command was used to calculate standardized proportions. Data were complete on all variables. The CHOP IRB approved the study and waived the requirement for consent from individual girls/families and clinicians.

Results

Study Population and Visit-Level Characteristics

A total of 17,016 adolescent girls were included in this study (Figure 1). The study included 32,472 visits (14,247 preventive, 18,225 acute). Table 1 presents visit-level characteristics. The numbers of girls and visits were similar across study arms. Of the 22,486 girls in the overall clinical trial, 5,470 did not have a preventive or acute visit during the study period and were excluded from this analysis (Figure 1). One hundred forty-five nurse/medical assistant–only visits were excluded.

Captured Opportunities for Vaccine Receipt

Eligible adolescents received a dose of the HPV vaccine at 36% of preventive visits and 4% of acute visits ($p<0.001$). Captured immunization opportunities were lower for HPV-1 than for later doses and much lower at acute than preventive visits; adolescents received HPV-1 at 25% of preventive and 1% of acute visits, respectively, compared to 79% and 18% for HPV-2 and 84% and 13% for HPV-3 ($p<0.001$ for all comparisons between preventive and acute visits).

Overall, the clinician-only intervention was more effective than the family-only intervention for increasing captured HPV vaccination opportunities at preventive visits (Table 2). The clinician-only intervention improved captured opportunities by 8.5 percentage points (95% CI=2.2, 14.7) for HPV-1, whereas the family-focused intervention fared no better than no intervention. Similarly, the combined intervention improved captured vaccination opportunities for HPV-1 by 9.7 percentage points (95% CI=3.8, 15.5) compared to no intervention. For HPV-2, neither intervention improved vaccination rates. For HPV-3, the clinician-only study arm experienced a significant increase of 6.2 percentage points (95% CI=1.9, 10.6) relative to no intervention. The combined group had a marginally significant improvement of 3 percentage points (95% CI=–0.1, 6.6), whereas the family-only intervention was not significantly different from no intervention. In analyses restricted only to the 5,033 visits (16% of total visits) at which at least one vaccine other than HPV was received, results were similar (data not shown).

At acute visits, both the clinician-only and combined intervention significantly improved captured opportunities

Table 1. Visit characteristics for girls due for the HPV vaccine, by study arm[a]

Variable	Overall	No. of visits (%)			
		Combined intervention	Clinician only	Family only	No intervention
Total girls	17,016	4,190	4,185	4,356	4,285
Total visits	32,472	7,742	7,952	8,490	8,288
PATIENT CHARACTERISTICS					
Age group (years)					
11–13	20,547 (63)	4,993 (64)	5,004 (63)	5,288 (62)	5,262 (63)
14–17	11,925 (37)	2,749 (36)	2,948 (37)	3,202 (38)	3,026 (37)
Race					
Black	8,372 (26)	2,260 (29)	2,194 (27)	1,972 (23)	1,946 (23)
White	20,240 (62)	4,713 (61)	4,897 (62)	5,327 (63)	5,303 (64)
Other	3,860 (12)	769 (10)	861 (11)	1,191 (14)	1,039 (13)
Hispanic	716 (2)	215 (3)	210 (3)	158 (2)	133 (2)
Private insurance	26,674 (82)	6,516 (84)	6,668 (84)	6,789 (80)	6,701 (81)
Prior oral contraceptives	905 (3)	253 (3)	230 (3)	186 (2)	236 (3)
CLINICIAN CHARACTERISTICS					
Practice location					
Urban	4,982 (15)	1,136 (15)	1,065 (13)	1,457 (17)	1,324 (16)
Suburban	27,490 (85)	6,606 (85)	6,887 (87)	7,033 (83)	6,964 (84)
Provider type					
Pediatrician	26,254 (81)	5,891 (76)	6,077 (77)	7,223 (85)	7,063 (85)
Nurse practitioner	5,476 (17)	1,697 (22)	1,701 (21)	1,035 (12)	1,043 (13)
Trainee	742 (2)	154 (2)	174 (2)	232 (3)	182 (2)
VISIT CHARACTERISTICS					
Visit type[b]					
Preventive[c]	14,247 (44)	3,556 (46)	3,445 (43)	3,756 (44)	3,490 (42)
Acute[d]	18,225 (56)	4,186 (54)	4,507 (57)	4,734 (56)	4,798 (58)
Excluded visits[e]	145 (<1)	55 (<1)	55 (1)	22 (<1)	13 (<1)
Other vaccine given at visit	5,033 (16)	1,293 (17)	1,259 (16)	1,269 (15)	1,212 (15)
Season of visit					
Spring	8,030 (25)	1,908 (25)	1,903 (24)	2,124 (25)	2,095 (25)
Summer	8,419 (26)	2,052 (27)	2,218 (28)	2,110 (25)	2,039 (25)
Fall	8,778 (27)	2,124 (27)	2,093 (26)	2,343 (28)	2,218 (27)
Winter	7,245 (22)	1,658 (21)	1,738 (22)	1,913 (22)	1,936 (23)

[a]All characteristics are presented at the visit level (i.e., number of visits with girls aged 11–13) because the visit was the unit of all analyses.
[b]The denominator for visit type is 32,587, of which 32,472 visits total were included in the analysis.
[c]Preventive visits included those with Current Procedural Terminology (CPT) codes 99383, 99384, 99393, and 99394.
[d]Acute visits include those with CPT codes 99201–99205, 99211–99215, 99242–99245.
[e]Excluded visits included nurse- or medical assistant–only and procedure-only visits.

Table 2. Standardized proportions[a] of captured HPV vaccination opportunities at preventive and acute visits

Study arm	Preventive visits			Acute visits		
	HPV-1 (*n*=11,653 visits)	HPV-2 (*n*=1,170 visits)	HPV-3 (*n*=1,424 visits)	HPV-1 (*n*=14,638 visits)	HPV-2 (*n*=1,746 visits)	HPV-3 (*n*=1,841 visits)
Combined (% [*n*])	30.3 (869)	81.9 (231)	85.9 (309)	1.2 (49)	26.6 (124)	16.0 (71)
Clinician only (% [*n*])	29.1 (815)	79.4 (213)	89.1 (287)	1.4 (57)	19.2 (90)	18.8 (81)
Family only (% [*n*])	21.0 (661)	77.7 (243)	79.9 (293)	0.5 (16)	11.3 (46)	11.9 (54)
No intervention (% [*n*])	20.6 (589)	78.7 (242)	82.9 (311)	0.5 (18)	12.1 (47)	7.5 (38)
Percentage point differences (95% CI)						
Combined versus no intervention	**9.7 (3.8, 15.5)**	3.2 (−3.1, 9.6)	3.0 (−0.1, 6.6)	**0.7 (0.2, 1.1)**	**14.5 (9.1, 19.8)**	**8.5 (4.2, 12.9)**
Clinician only versus no intervention	**8.5 (2.2, 14.7)**	0.7 (−5.6, 6.9)	**6.2 (1.9, 10.6)**	**0.9 (0.1, 1.6)**	**7.1 (1.0, 13.2)**	**11.3 (5.6, 17.1)**
Family only versus no intervention	0.4 (−1.7, 2.4)	−1.0 (−7.3, 5.3)	−3.0 (−6.8, 0.9)	0.0 (−0.4, 0.4)	−0.8 (−4.8, 3.3)	**4.4 (0.1, 8.7)**
Clinician only versus family only	**8.1 (2.6, 13.7)**	1.7 (−4.5, 7.8)	**9.2 (4.1, 14.4)**	**0.9 (0.1, 1.7)**	**7.9 (1.7, 14.0)**	**6.9 (0.5, 13.4)**
Combined versus clinician only	1.2 (0.0, 2.5)	2.5 (−2.6, 7.8)	−3.2 (−6.9, 0.5)	−0.2 (−0.7, 0.4)	**7.4 (1.7, 13.0)**	−2.8 (−7.5, 1.9)
Combined versus family only	**9.3 (4.2, 14.4)**	4.2 (−2.0, 10.5)	**6.0 (1.2, 10.8)**	**0.7 (0.3, 1.2)**	**15.3 (9.9, 20.7)**	4.1 (−1.1, 9.3)

Note: Boldface indicates statistical significance ($p<0.05$).
[a]Standardized proportions were transformed using marginal standardization[34] from multivariable logistic regression models with robust variance estimates accounting for clustering at the practice level and adjusting for included covariates. Proportions were similar in the unadjusted results (data not shown). The actual number of visits at which each vaccine dose was received is provided next to the standardized proportions.

for all three doses of the HPV vaccine relative to no intervention ($p<0.05$ for all comparisons) (Table 2). For HPV-1, the combined intervention increased captured opportunities by only 0.7 percentage points (95% CI=0.2, 1.1) and the clinician-only by 0.9 percentage points (95% CI=0.1, 1.6). The combined intervention was significantly better than the clinician-only for HPV-2. The family-only intervention increased captured opportunities compared to no intervention only for HPV-3.

At preventive visits, immunization opportunities were captured approximately twice as frequently for HPV-1 at urban practices compared to suburban (Table 3). The effect of the clinician-focused intervention was larger for HPV-1 at suburban versus urban practices; the combined and clinician-only interventions increased captured opportunities by approximately 10 percentage points relative to no intervention at suburban, compared to increases of 2 percentage points for urban sites. In contrast, these large differences were not observed for HPV-2 and HPV-3 at preventive visits (Table 3).

At acute visits, captured vaccination opportunities were higher overall at urban than suburban practices, though still much lower than at preventive visits. The clinician-only intervention increased captured opportunities by a greater magnitude for all three doses in urban versus suburban practice settings (Table 3). There was no significant interaction between study arm and age group in any analysis (all $p>0.2$).

Discussion

In this analysis of the effect of automated decision support directed at families, clinicians, or both on captured opportunities for HPV vaccination, the clinician-focused intervention had a greater effect than the family-focused one. The clinician-focused intervention, either alone or in combination with the family-focused, improved captured opportunities relative to no intervention at both preventive and acute visits, whereas the family-focused intervention alone rarely resulted in a significant improvement. At preventive visits, the clinician-focused intervention better supported vaccine initiation at suburban sites, which had lower captured opportunities, compared to urban. Conversely, at acute visits, the clinician intervention increased captured opportunities more at urban than suburban practices.

Table 3. Standardized proportions[a] of captured immunization opportunities in urban versus suburban practice settings

Study arm	Urban			Suburban		
	HPV-1 (*n*=1,422 visits)	HPV-2 (*n*=538 visits)	HPV-3 (*n*=512 visits)	HPV-1 (*n*=10,231 visits)	HPV-2 (*n*=632 visits)	HPV-3 (*n*=912 visits)
A. PREVENTIVE VISITS						
Combined (% [*n*])	45.5 (148)	87.5 (83)	82.6 (96)	27.9 (721)	78.4 (148)	87.4 (213)
Clinician only (% [*n*])	45.1 (139)	82.2 (81)	87.5 (74)	26.5 (676)	76.5 (132)	89.6 (213)
Family only (% [*n*])	43.5 (186)	80.8 (144)	81.4 (128)	17.8 (475)	75.0 (99)	78.9 (165)
No intervention (% [*n*])	43.4 (157)	81.4 (136)	82.8 (127)	17.7 (432)	76.5 (106)	83.0 (184)
Percentage point differences						
Combined versus no intervention	2.1 (−15.1, 19.3)	**6.1 (0.7, 11.6)**	−0.2 (−3.6, 3.2)	**10.2 (4.6, 15.7)**	1.9 (−9.7, 13.5)	4.4 (−0.5, 9.4)
Clinician only versus no intervention	1.7 (−16.9, 20.3)	0.8 (−0.9, 2.4)	**4.7 (0.9, 8.5)**	**8.8 (2.9, 14.6)**	0.0 (−12.2, 12.1)	**6.6 (0.4, 12.9)**
Family only versus no intervention	0.1 (−10.1, 10.3)	−0.6 (−4.1, 2.9)	−1.4 (−5.3, 2.4)	0.1 (−1.8, 2.0)	−1.5 (−15.0, 11.9)	−4.1 (−10.2, 2.1)
Clinician only versus family only	1.6 (−7.5, 10.8)	1.4 (−3.6, 6.4)	**6.1 (3.8, 8.5)**	**8.7 (3.5, 13.9)**	1.5 (−9.2, 12.2)	**10.7 (2.8, 18.6)**
Combined versus clinician only	0.4 (−2.1,2.9)	**5.3 (0.6, 10.1)**	**−4.9 (−5.7, −4.1)**	1.4 (0.0, 2.9)	1.9 (−5.5, 9.3)	−2.2 (−7.1, 2.7)
Combined versus family only	2.0 (−5.2, 9.3)	6.7 (−0.7, 14.2)	1.2 (−0.9, 3.4)	10.1 (5.2, 14.9)	3.4 (−6.9, 13.7)	**8.5 (1.3, 15.7)**

Study arm	HPV-1 (*n*=1,388 visits)	HPV-2 (*n*=587 visits)	HPV-3 (*n*=535 visits)	HPV-1 (*n*=13,250 visits)	HPV-2 (*n*=1,159 visits)	HPV-3 (*n*=1,306 visits)
B. ACUTE VISITS						
Combined (% [*n*])	4.5 (20)	34.1 (47)	19.3 (23)	0.9 (29)	23.9 (77)	15.1 (48)
Clinician only (% [*n*])	7.8 (32)	29.9 (40)	29.6 (30)	0.7 (25)	14.6 (50)	16.0 (51)
Family only (% [*n*])	2.7 (6)	11.9 (19)	17.3 (28)	0.3 (10)	11.1 (27)	8.9 (26)
No intervention (% [*n*])	2.8 (8)	16.8 (24)	13.0 (18)	0.3 (10)	9.5 (23)	5.3 (20)
Percentage point differences (95% CI)						
Combined versus no intervention	1.7 (−0.4, 3.9)	**17.3 (6.0, 28.7)**	6.3 (−0.5, 13.1)	**0.6 (0.1, 1.1)**	**14.5 (8.7, 20.3)**	**9.8 (4.9, 14.7)**
Clinician only versus no intervention	**5.0 (2.6, 7.4)**	**13.1 (10.4, 15.9)**	**16.6 (4.4, 28.8)**	0.4 (−0.2, 1.1)	5.1 (−1.3, 11.5)	**10.7 (5.3, 16.1)**

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Table 3. Standardized proportions[a] of captured immunization opportunities in urban versus suburban practice settings *(continued)*

Study arm	HPV-1 (*n*=1,388 visits)	HPV-2 (*n*=587 visits)	HPV-3 (*n*=535 visits)	HPV-1 (*n*=13,250 visits)	HPV-2 (*n*=1,159 visits)	HPV-3 (*n*=1,306 visits)
Family only versus no intervention	−0.1 (−0.4, 3.9)	**−4.9 (−5.7, −4.1)**	**4.3 (3.8, 4.8)**	0.0 (−0.4, 0.3)	1.6 (−3.6, 6.9)	3.6 (−2.8, 10.0)
Clinician only versus family only	**5.1 (3.4, 6.7)**	**18.0 (16.1, 20.0)**	**12.3 (0.3, 24.3)**	0.4 (−0.2, 1.1)	3.5 (−3.8, 10.7)	**7.1 (0.3, 13.9)**
Combined versus clinician only	**−3.2 (−5.1, −1.4)**	4.2 (−7.8, 16.3)	**−10.3 (−17.4, −3.1)**	0.2 (−0.2, 0.5)	**9.3 (2.1, 16.6)**	−0.9 (−6.5, 4.7)
Combined versus family only	**1.8 (1.1, 2.6)**	**22.2 (10.7, 33.7)**	2.0 (−4.4, 8.4)	**0.6 (0.0, 1.1)**	**12.8 (6.0, 19.6)**	6.2 (−0.4, 12.8)

Note: Boldface indicates statistical significance ($p<0.05$).
[a]Standardized proportions were transformed using marginal standardization[34] from multivariable logistic regression models with robust variance estimates accounting for clustering at the practice level and adjusting for included covariates. The actual number of visits at which each vaccine dose was received is provided next to the standardized proportions.

However, despite improvements, rates of captured opportunities remained low, particularly for vaccine initiation and vaccination at acute visits.

The results of this visit-level analysis of captured opportunities contrast with the results of the patient-level analysis of vaccination rates from the original trial. In the patient-level analysis,[25] clinician-focused decision support alone was effective for improving HPV initiation, but not follow-up doses, whereas family-focused reminder calls fostered receipt of the second and third dose, but not initiation. The combined intervention significantly improved vaccination rates for all three doses. The results presented in this manuscript suggest that alerts for clinicians appearing during office visits represent a stronger trigger for vaccine administration than phone calls prior to the visit.

Consistent with a substantial literature[36–44] indicating the importance of clinician recommendation and parental perception of clinician support for vaccine acceptance, the clinician-focused intervention was superior to the family-focused in preventing missed opportunities. The finding that clinician-focused decision support decreased missed opportunities suggests that the presence of the alert, in the context of the broader clinician intervention, may increase the likelihood that clinicians recommend the HPV vaccine to parents, leading to greater parental acceptance of vaccination. The results of a qualitative substudy of 162 families enrolled in this trial support this idea; in that study, parents of girls who attended intervention practices were significantly more likely to report that their clinician discussed the HPV vaccine than those attending practices not receiving the clinician intervention.[45]

Further work is needed to fully explain why the benefit of the clinician intervention differed between urban and suburban sites. At preventive visits, the clinician intervention increased captured opportunities for HPV-1 more in the suburban sites, where captured opportunities were less common, compared to urban sites. These results suggest that alerts, education, and feedback were enough to increase the consistency with which suburban pediatricians recommended HPV-1, leading to large improvements from low rates in the no intervention group. Captured opportunities were already much higher for HPV-1 at urban practices, potentially resulting in a ceiling effect, which may explain the diminished effect of the intervention.

At acute visits, clinician-focused decision support may have been more effective in the urban setting because it was consistent with existing workflows, a known requirement for effective decision support that supported acute visit vaccination.[46,47] As has been documented previously,[13] providers in urban settings also may have

encountered less resistance from families to the vaccine, increasing their willingness to recommend the vaccine at time-limited acute visits.

Despite the significant impact of the clinician-focused intervention on improving captured immunization opportunities, many opportunities for HPV vaccination were missed in this study, particularly at acute visits and for vaccine initiation. At acute visits, missed opportunities are particularly common for several reasons: providers may prefer to focus on the acute problem, lack time to address vaccination, and be concerned that vaccination during acute visits reduces attendance at subsequent preventive visits.[46,48,49] The intervention in this study alerted clinicians that vaccines were due, but may not have fully addressed these barriers. In addition, many families continue to question vaccine safety, effectiveness, and necessity for younger adolescents.[13,14,38] As a result, many choose to delay HPV vaccine initiation or refuse it outright.[13]

The clinician-focused intervention's educational component was designed to provide clinicians with the skills to address these concerns, and the feedback and alerts to remind them to discuss the vaccine at each opportunity. However, success depended upon clinicians' using these skills and families' willingness to accept the vaccine, and results from this study suggest that some families could not be convinced. Given the persistently low number of captured opportunities despite a multicomponent intervention, complementary strategies that address known barriers at the health system, practice, family, and clinician levels and enlist quality improvement methods may be needed to further decrease missed opportunities.[50]

This study had several limitations. The study was conducted within one health system in one region of the country. However, the sample of adolescent girls was large and diverse, enhancing generalizability. Additionally, although analyses controlled for clinically relevant covariates and found minimal differences between unadjusted and standardized results, it is possible that the inclusion of unmeasured confounders may have affected results. For example, information on family structure was not captured. Finally, although clinically important, the outcome studied in this paper was not specified prior to randomization.

Conclusions

This trial demonstrated the value of a clinician-focused intervention to improve captured HPV vaccination opportunities among adolescent girls at both preventive and acute visits. Even with the improvements associated with the clinician-focused intervention, missed opportunities for HPV vaccinations were common. These results suggest that although clinical decision support in the context of a broader clinician-focused intervention is an effective method of reducing HPV missed opportunities, complementary strategies are needed to further reduce missed opportunities for HPV vaccination among adolescent girls.

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Dr. Fiks has the following conflict of interest: he is a co-inventor of the "Care Assistant" that was used to provide the clinician-focused, point-of-care decision support in this study. He holds no patent on the software and has earned no money from this invention. No licensing agreement exists. After this study, Dr. Fiks received an Independent Research Grant from Pfizer for an unrelated topic.

Dr. Grundmeier has the following conflicts of interest: he is a co-inventor of the "Care Assistant" that was used to provide the clinician-focused, point-of-care decision support in this study. He holds no patent on the software and has earned no money from this invention. No licensing agreement exists. Additionally, a member of Dr. Grundmeier's family received speaker's fees from Merck.

Dr. Feemster has the following conflicts of interest: she received an honorarium from Pfizer for participation on an advisory board regarding changing attitudes toward vaccines among clinicians in April 2012. Additionally, she received an honorarium from Abbot Laboratories for serving as a speaker at Influenza Forum Europe in November 2012.

To manage conflicts of interest, data management and analyses were overseen and results were independently reviewed and verified by one of the authors (RL) who had no conflict of interest.

The remaining authors have no other conflicts of interest or financial relationships relevant to this article to disclose.

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Appendix

Supplementary data

Supplementary data associated with this article can be found at http://dx.doi.org/10.1016/j.amepre.2014.08.010.