

ORIGINAL RESEARCH

The Effect of Offering Pneumococcal Vaccines During Specialty Care on Vaccination Rates in Patients Receiving Immunosuppressive Therapy

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ABSTRACT

Purpose: To determine whether clinician-led immunization education with immediate onsite vaccination availability will increase pneumococcal immunizations during specialty care.

Methods: We used a controlled before and after quasi-experimental design to retrospectively evaluate quality improvement (QI) project effectiveness. The project included two clinics. Clinic #1 was a part of the county hospital system and offered comprehensive care. Clinic #2 was a university clinic that hosted a private practice and a dermatology resident continuity clinic. Resident continuity clinics are structured to enable residents to develop longitudinal relationships with patients with skin disease. Patients within each of these clinics were subject to the intervention or usual care based on their treating physician. The intervention included clinician-provided verbal immunization recommendations, dialogue exploring and addressing patients' immunization concerns, and immediate availability of vaccine and administration. The main measure of outcome was pneumococcal immunization status after QI intervention.

Results: Our analysis included 201 patients with planned or existing immunosuppressive medication regimens attending an initial or follow-up dermatology visit (aged 0-64 years [82.1%], aged ≥65 years [17.9%]; male [34.3%], female [65.6%]). Of these, 146 [72.6%] were in the QI group and 55 [27.4%] in the comparison group. While we identified no significant QI/comparison group differences in immunization status at initial observation ($p=0.329$), immunization status differed significantly by group at the final observation ($p<0.001$). The QI group had a significant increase in immunization status compared to the comparison group ($p<0.001$). Overall, 81.4% (95% CI: 73.6, 87.3) of patients in the QI group without full immunization at initial observation received at least one vaccination by the final observation, while we observed no change in immunization status for the comparison group from initial to final observation.

Conclusion: These data demonstrate that immunization coverage in patients on immunosuppressive medications can be markedly improved by clinician recommendation with immediate availability of the pneumococcal vaccine during specialty care. Wider adoption of this model and its adaptation to other immunizations and settings is an important opportunity to reduce vaccine-preventable illness, including COVID-19, and improve population health.

INTRODUCTION

Morbidity and mortality from vaccine-preventable illnesses are higher among patients on immunosuppressive treatment.¹⁻⁷ Immunosuppressive therapies increase the risk of infections by at least 2-fold compared to non-immunosuppressed individuals.^{6,8} The incidence rate of invasive pneumococcal disease is approximately 6-fold higher in patients with chronic inflammatory disease receiving immunosuppressive medications when compared to healthy individuals.⁹ Patients receiving immunosuppressive medications are recommended to receive routine pneumococcal immunizations to reduce infectious complications.^{10,11} These recommendations are not completely implemented worldwide. Studies conducted around the world find that persons on immunosuppressive medications and persons with chronic conditions commonly treated with such medications are undervaccinated, with pneumococcal vaccination rates ranging from 0% in Morocco to 56.5% in France.¹²⁻¹⁵ More effectively addressing this disparity is key to reducing morbidity, mortality, and economic losses from vaccine-preventable disease.^{6,12,16,17}

There are many reasons vaccination coverage is low in adult and immunosuppressed populations.¹⁸⁻²⁰ Most immunosuppressed patients cited lack of physician recommendation for the reason for their being unimmunized.^{18,21,22} Other concerns include vaccine safety and efficacy.²⁰ The most common reason cited by physicians for not immunizing was forgetting to recommend.^{19,20} Another clinician barrier to immunizing is uncertainty of vaccination schedule.¹⁸ In addition to patient and clinician barriers there are

system immunization barriers including fragmented delivery systems, uneven access, and lack of immunization coordination. Vaccination is widely available from pharmacies, urgent care, primary care, specialty, and public health clinics. There is no system for routine communication between these sites providing immunizations and an adult vaccine registry. This can lead to both patient and clinician uncertainty as to an individual's vaccine status. Often as a result of this uncertainty, a patient leaves the office without immunization but with plans for future immunization.

Recommendations for where vaccination should occur are either absent or it is recommended that they be given by a primary care clinician.²³⁻²⁵ General practitioners surveyed about who should provide immunizations for patients on immunosuppressive medications believed the prescribing specialist should monitor the immunizations.²⁶ Surveys of Irish rheumatologists showed 57% thought general practitioners should be responsible for providing these patients with immunizations.²⁷ These data illustrate there is discordance about who should ultimately be responsible for vaccinating immunosuppressed patients.

The CDC Advisory Committee on Immunization Practices (ACIP) has recommended several strategies to increase vaccine adherence.²⁸ Useful methods include direct patient communications and organizational changes such as separate clinics devoted to prevention, planned preventive medicine visits, or the use of non-physician staff to do preventative medicine visits.^{29,30} Absent or weak immunization recommendations from clinicians are a primary cause of low immunization uptake.³¹

Similar to other organizations, our dermatology practice observed low pneumococcal immunization coverage among patients receiving immunosuppressive care. The ACIP states that the two most important predictors of immunization acceptance among adults are the healthcare provider's recommendation and availability of the vaccine during the same visit.³² We designed a quality improvement (QI) project around this logic, hypothesizing that clinician-led immunization education with immediate onsite vaccination availability will increase receipt of pneumococcal immunizations during specialty care. We evaluated the results of the QI project and present our findings in this report.

METHODS

This project was approved as exempt category research by the North Texas Regional Institutional Review Board.

Study Design and Participants

We used a before and after quasi-experimental design to retrospectively evaluate our QI project to increase acceptance of pneumococcal immunizations in immunosuppressed patients³³. Our evaluation included all patients who were newly or previously prescribed chronic systemic immunosuppressive therapy that visited any of four dermatology practices during a defined period. Therapies of interest included biologics, antimetabolites, oral corticosteroids, and other immunosuppressive medications.

The four dermatology practices were in two clinics; one dermatology practice in each clinic administered the QI intervention while the other practice provided standard care. Patients were subject to the intervention or

usual care based on their treating physician (eMethods). All eligible patients seeking care between September (Clinic #1) or November (Clinic # 2) of 2019 through March 30, 2020 were included in analyses. All were followed for immunization completion through July 2020.

Both clinics provide care to patients of predominately lower socioeconomic status in Tarrant County, Texas. In 2019, Tarrant County's estimated population was 2,102,515 residents across its 863.6 square miles; 51.8% of whom were white, 26.7% Hispanic or Latino, 14.5% Black or African American, 4.6% Asian, and 2.4% other³⁴.

Standard Care

Prior to the QI intervention, PVC13 and PPSV23 pneumococcal vaccine was on the formulary of both institutions and clinic staff were familiar with vaccine administration and EMR documentation. However, dermatologists recommended that immunosuppressed patients see their primary clinicians to update pneumococcal vaccinations.

Quality Improvement Intervention

As a QI intervention, the physician provided each eligible patient with immunization recommendations based on their immunization status and ACIP guidelines. Educational elements included the increased risk of infection associated with immunosuppressive medications, benefits of immunization to reduce this risk, and addressing any concerns the patients had about the vaccine²⁸. Patients were given an opportunity to receive pneumococcal immunizations immediately after the physician education.

Data Source and Measures

Data for all variables were retrospectively collected from electronic medical records

(EMR). Patients were also queried about immunizations received from outside the practice, either during routine visits or in follow-up telephone calls.

The primary outcome measure was immunization status. We created a three-level ordinal immunization status variable based on ACIP guidelines²⁸, categorizing patients as having no, partial, or full immunization. Immunization status was evaluated at two points in time: 1) the first visit to the dermatology clinic during the project period (initial observation), and 2) the end of the observation period (final observation). Data from the two clinics were combined for analysis, so patients were in one of two groups: 1) the QI group, or 2) the comparison group. Thus, time and group were variables in our analyses.

Analyses included demographic, care delivery, and patient health variables. Demographic variables included gender, age, race/ethnicity. The care delivery variables included insurance status, use of translators, and past-year office-based healthcare visits to any clinician. Patient health variables included the number of comorbid conditions, the condition for which immunosuppressive medications were prescribed, the number and types of immunosuppressive medications used, and the number of pneumococcal vaccination indications other than medications and age.

Statistical Analyses

We analyzed differences between the QI and comparison groups in demographics, care delivery, health, or immunization status at initial observation. We calculated the unadjusted percentage of patients at each immunization level within each group at initial and final observation. We then used unadjusted and adjusted ordered logit difference-in-difference models to test for

significant changes in immunization levels for the two groups. The unadjusted model included group, time, and group by time interaction. The adjusted model added gender, age, insurance, a count of prior year office-based visits, visit type, and the number of indications for vaccination. Models accounted for non-independence of initial and final observations. The adjusted model was used to generate the average adjusted probabilities of persons in the QI and comparison group being at each level of immunization at initial and final observations (eMethods).

Additional analyses included an examination of associations between immunization levels at initial observation and the presence and duration of immunosuppressive medication use prior to initial observation. We also analyzed data for the subset of patients who were newly prescribed immunosuppressive medication during the project to evaluate the effectiveness of the intervention on this group. Last, we conducted analyses that included only persons in the QI group who were not fully immunized at initial observation to identify factors associated with non-receipt of a vaccination in this group (eMethods).

All statistical testing was two-sided and used Stata 14.2 [StataCorp; College Station, TX]. Significance was tested at $p < 0.05$.

RESULTS

Our analysis included 201 patients with planned or existing immunosuppression attending an initial or follow-up dermatology visit. Of these, 146 (72.6%; 91 from Clinic #1 and 55 from Clinic #2) were in the QI group and 55 (27.4%; 41 from Clinic #1 and 14 from Clinic #2) in the comparison group. While the comparison group contained a

Table 1. Characteristics of immunosuppressed patients included in analyses, total and by quality improvement (QI) versus comparison group.

Variable	Categories	Total	QI Group	Comparison Group	p-value ^a	
		n=201	n=146	n=55		
		Column % (95% CI)	Column % (95% CI)	Column % (95% CI)		
Pneumococcal immunization status at initial observation	No immunization	67.2 (60.3, 73.4)	69.9 (61.9, 76.8)	60.0 (46.4, 72.2)	0.329	
	Partially immunized	22.4 (17.1, 28.7)	18.5 (13.0, 25.7)	32.7 (21.5, 46.3)		
	Fully immunized	10.5 (6.9, 15.5)	11.6 (7.3, 18.0)	7.3 (2.7, 18.1)		
Gender	Female	65.6 (58.8, 72.0)	66.4 (58.3, 73.7)	63.6 (50.0, 75.4)	0.709	
	Male	34.3 (28.0, 41.2)	33.6 (26.3, 41.7)	36.4 (24.6, 50.0)		
Age	<=34	17.9 (13.2, 23.9)	19.9 (14.1, 27.2)	12.7 (6.1, 24.6)	0.307	
	35-44	17.9 (13.2, 23.9)	19.9 (14.1, 27.2)	12.7 (6.1, 24.6)		
	45-54	20.9 (15.8, 27.1)	17.8 (12.4, 24.9)	29.1 (18.5, 42.6)		
	55-64	25.4 (19.8, 31.9)	24.7 (18.3, 32.4)	27.3 (17.0, 40.7)		
	>=65	17.9 (13.2, 23.9)	17.8 (12.4, 24.9)	18.2 (10.0, 30.8)		
Race/Ethnicity	White non-Hispanic	37.8 (31.3, 44.8)	40.4 (32.7, 48.6)	30.9 (20.0, 44.4)	0.162	
	Black non-Hispanic	23.9 (18.4, 30.3)	19.9 (14.1, 27.2)	34.5 (23.1, 48.1)		
	Hispanic	31.8 (25.7, 38.7)	33.6 (26.3, 41.7)	27.3 (17.0, 40.7)		
	Other race/ethnicity	6.5 (3.8, 10.9)	6.2 (3.2, 11.5)	7.3 (2.7, 18.1)		
Primary insurance	Private	11 (7.3, 16.1)	11.6 (7.3, 18.0)	9.1 (3.8, 20.3)	0.176	
	Public (Medicare or Medicaid)	52.2 (45.3, 59.1)	56.2 (47.9, 64.1)	41.8 (29.4, 55.3)		
	County program	26.9 (21.1, 33.5)	23.3 (17.1, 30.9)	36.4 (24.6, 50.0)		
	Uninsured	10 (6.5, 15.0)	8.9 (5.2, 14.8)	12.7 (6.1, 24.6)		
Patient used translator^b	Yes	19.9 (13.2, 23.9)	17.8 (12.4, 24.9)	18.2 (10.0, 30.8)	0.951	
Count of past year office-based contacts (all provider specialties)	0-3 visits	23.4 (18.0, 29.8)	28.1 (21.3, 36.0)	10.9 (4.9, 22.5)	0.068	
	4-8 visits	31.3 (25.3, 38.1)	29.5 (22.6, 37.4)	36.4 (24.6, 50.0)		
	9-14 visits	27.4 (21.6, 34.0)	26.7 (20.1, 34.5)	29.1 (18.5, 42.6)		
	>=15 visits	17.9 (13.2, 23.9)	15.8 (10.7, 22.7)	23.6 (14.1, 36.8)		
Visit type at initial observation	Initial	23.4 (18.0, 29.8)	19.2 (13.5, 26.5)	34.5 (23.1, 48.1)	0.022	
	Follow-up	76.6 (70.2, 82.0)	80.8 (73.5, 86.5)	65.5 (51.9, 76.9)		
Number of comorbid conditions^b	None	14.4 (10.2, 20.0)	15.1 (10.1, 21.9)	12.7 (6.2, 24.5)	0.681	
	1-3 conditions	47.8 (40.9, 54.7)	48.6 (40.6, 56.8)	45.5 (32.8, 58.7)		
	4 or more conditions	37.8 (31.3, 44.8)	36.3 (28.9, 44.4)	41.8 (29.5, 55.2)		
Immunosuppressive medications used prior to initial observation^c	Yes	83.1 (77.2, 87.7)	83.6 (76.6, 88.8)	81.8 (69.2, 90.0)	0.769	
Condition for which individual was prescribed immunosuppressive medication(s) (all provider specialties)	Psoriasis with or without psoriatic arthritis	70.2 (63.4, 76.1)	69.2 (61.1, 76.2)	72.7 (59.3, 83.0)	0.474	
	Hidradenitis suppurativa	9.5 (6.1, 14.4)	9.6 (5.7, 15.6)	9.1 (3.8, 20.3)		
	Connective tissue disease	8.5 (5.3, 13.2)	9.6 (5.7, 15.6)	5.5 (1.7, 15.8)		
	Rheumatoid arthritis	5.5 (3.0, 9.7)	4.8 (2.3, 9.8)	7.3 (2.7, 18.1)		
	Vesiculobullous disease	4 (2.0, 7.8)	4.8 (2.3, 9.8)	1.8 (0.2, 12.1)		

	Atopic dermatitis	1 (0.2, 3.9)	0.7 (0.1, 4.8)	1.8 (0.2, 12.1)	
	Inflammatory bowel disease	0.5 (0.1, 3.5)	0.7 (0.1, 4.8)	0	
	Chronic lichenoid inflammatory disease	0.5 (0.1, 3.5)	0.7 (0.1, 4.8)	0	
	Organ transplant	0.5 (0.1, 3.5)	0	1.8 (0.2, 12.1)	
Current number of immunosuppressive medications prescribed (all provider specialties)	1 medication	80.6 (74.5, 85.5)	80.1 (72.8, 85.9)	81.8 (69.2, 90.0)	0.788
	2 medications	17.4 (12.7, 23.3)	17.8 (12.4, 24.9)	16.4 (8.7, 28.8)	
	3 medications	2 (0.7, 5.2)	2.1 (0.7, 6.2)	1.8 (0.2, 12.1)	
Prescribed biologics^d	Yes	80.1 (73.9, 85.1)	82.2 (75.1, 87.6)	74.5 (61.3, 84.4)	0.226
Prescribed antimetabolites, corticosteroids, or other immunosuppressive^d	Yes	31.3 (25.3, 38.1)	30.8 (23.8, 38.8)	32.7 (21.6, 46.1)	0.795
Number of indications for immunization other than medication(s) and age^d	0 indications	45.3 (38.5, 52.2)	44.5 (36.6, 52.7)	47.3 (34.4, 60.5)	0.765
	1 indication	32.8 (26.6, 39.7)	33.6 (26.3, 41.7)	30.9 (20.0, 44.4)	
	2 indications	14.9 (10.6, 20.6)	14.4 (9.5, 21.1)	16.4 (8.7, 28.8)	
	3 indications	6 (3.4, 10.3)	6.9 (3.7, 12.3)	3.6 (0.9, 13.7)	
	4 indications	1 (0.2, 3.9)	0.7 (0.1, 4.8)	1.8 (0.2, 12.1)	

^a Significance was evaluated using Pearson's chi-squared tests and Wilcoxon rank-sum tests for categorical and ordinal variables, respectively.

^b Comorbid conditions included asthma, CAD, cancer, chronic pain, COPD, chronic renal failure, diabetes, high cholesterol, hypertension, hypothyroidism, psychiatric, seizures GERD, OAA, or other conditions.

^c Dichotomous yes/no variables only display data for the "Yes" category.

^d Indications include heart disease (CHF or CAD), diabetes, lung disease (COPD or asthma), chronic renal failure, or being a current smoker. Possible range 0-5, actual range 0-4

Table 2. Unadjusted and adjusted column percentages reflecting immunization status by group and point in time. N=201.

	QI Group (N=146)		Comparison Group (n=55)		p-value	QI Group (N=146)		Comparison Group (n=55)		p-value
	Unadjusted Column Percentages (95% CI)					Adjusted Column Percentages ^a (95% CI)				
Immunization Status	Initial observation	Final observation	Initial observation	Final observation		Initial observation	Final observation	Initial observation	Final observation	
No immunization	69.9 (61.9, 76.8)	13.7 (9.0, 20.4)	60.0 (46.4, 72.2)	60.0 (46.4, 72.2)	<0.001	66.3 (59.8, 72.7)	16.1 (10.9, 21.3)	62.1 (53.6, 71.6)	62.1 (53.6, 71.6)	<0.001
Partially immunized	18.5 (13.0, 25.7)	47.9 (39.9, 56.1)	32.7 (21.5, 46.3)	32.7 (21.5, 46.3)		26.1 (21.3, 30.9)	43.2 (37.0, 49.4)	28.7 (21.4, 36.0)	28.7 (21.4, 36.0)	
Fully immunized	11.6 (7.3, 18.0)	38.4 (30.8, 46.6)	7.3 (2.7, 18.1)	7.3 (2.7, 18.1)		7.7 (3.9, 11.4)	40.6 (0.34, 0.47)	9.2 (5.0, 13.4)	9.2 (5.0, 13.4)	

^a Adjusted column percentages are the average predicted probabilities calculated based on results of a multivariable ordered logit model (see Table 4 in the Supplement); probabilities multiplied by 100 and expressed as percentages

higher proportion of new patients (p -value = 0.022), we found no significant differences between QI and comparison groups for other demographic, care delivery, or health variables ($p > 0.05$ for each; Table 1).

While our unadjusted analyses identified no significant group differences in immunization status at initial observation ($p = 0.329$; Table 1), immunization status differed significantly by QI/comparison group at the final observation ($p < 0.001$; Table 2). Of the 102 patients in the QI group with no pneumococcal immunizations at initial observation, 80.4% (95% CI: 71.4%, 87.1%) received at least one pneumonia vaccination by the final observation. For the 27 patients in the QI group with partial immunization at project initiation, 85.2% (95% CI: 65.9%, 94.5%) received at least one pneumonia vaccination. Overall, 81.4% (95% CI: 73.6, 87.3) of patients in the QI group without full immunization at initial observation received at least one vaccination by the final observation. Pneumococcal immunization statuses did not change during the project period within the comparison group (Table 2).

Regression analyses identified that the QI group had a significant change in immunization status compared to the comparison group (Table 2; unadjusted difference-in-difference $p < 0.001$, Table 3). Immunization acceptance patterns for the subset of 34 patients not previously on immunosuppression who were prescribed immunosuppressive medication during the project were similar. Of those with new prescriptions, 75% (18/24; 95% CI: 53.0, 88.9) of the QI group and 0% (0/10) of the comparison group received at least one pneumococcal immunization by final observation ($p < 0.001$; data not shown).

Table 3: Results of unadjusted ordered logit model examining differences in immunization status for the QI group versus comparison group at initial versus final observation. Analysis accounts for repeated measures ($n = 201$).

	Odds Ratio (OR)	95% Confidence Interval of OR		p-value
Group				
<i>Comparison group</i>	1.00	(ref)		
<i>QI group</i>	0.72	0.38	1.37	0.321
Time				
<i>Initial observation</i>	1.00	(ref)		
<i>Final observation</i>	1.00	.	.	.
Interaction				
<i>Group*Time</i>	10.14	6.71	15.34	<0.001

Findings were similar after adjusting for demographic, clinical, and other factors, with a significant change in immunization status at final observation among patients in the QI group and no change in the comparison group (Table 2). Consequently, there was a significant interaction between group and time ($p = < 0.001$; Table 4). Figure 1 visualizes the predicted probabilities of persons in the QI group being immunized at initial versus final observation. For the QI group, the predicted probabilities of having no, partial, or full immunizations at initial observation were 0.66, 0.26, and 0.08, respectively. At the time of final observation for the QI group, the predicted probabilities of having no, partial, or full immunizations were 0.16, 0.43, and 0.41, respectively. Predicted probabilities for the comparison group of having no, partial, or full immunizations at initial observation were 0.62, 0.29, and 0.09, respectively and did not change during the project (Table 2).

Controlling for time, group, and other factors, patients 65 years of age or older had significantly greater odds of having a higher immunization status compared to

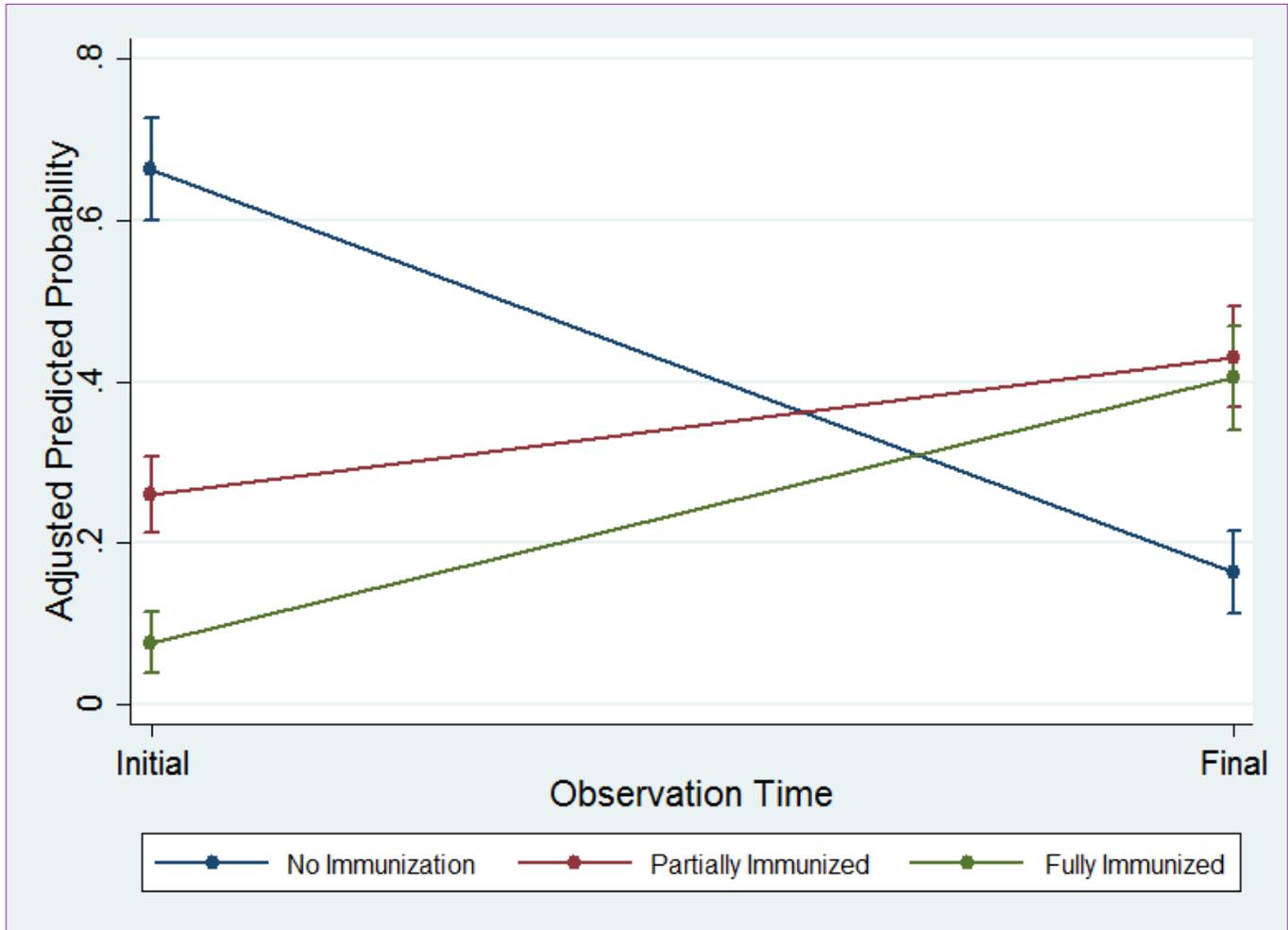


Figure 1. Adjusted average predicted probabilities of persons in the QI group being unimmunized, partially immunized, and fully immunized at initial and final observations. Probabilities were generated based on the results of the multivariable ordered logit model detailed in eTable 2 of the Supplement.

younger persons ($p < 0.001$). A significant association was also found between the number of risk factors for pneumonia and higher immunization statuses ($p = 0.034$). Conversely, the number of prior office visits was not significantly associated with immunization level after controlling for other factors (Table 4; $p > 0.05$ for all levels).

Our analyses investigating variations in the intervention's effectiveness indicated uninsured patients were less likely to receive a vaccination relative to insured patients (unadjusted $p = 0.007$, adjusted $p = 0.015$; Table 5). Further, regardless of group, immunosuppressive medication use before

initial observation was not significantly associated with immunization status. This was true whether medication use was dichotomized ($z = -0.35$, $p = 0.725$) or categorized based on immunosuppression duration ($r^2 = 0.11$, $p = 0.119$; Table 6).

DISCUSSION

Pneumococcal immunizations are indicated for adults at risk of severe disease, hospitalization, and death from pneumococcal illnesses²⁸. This public health recommendation is incompletely implemented worldwide leaving a large gap

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Table 4. Results of multivariable ordered logit model. The model's dependent variable is immunization status; the main predictor variables are group, time and the group by time interaction. Analysis accounts for repeated measures (n=201).

	Odds Ratio (OR)	95% Confidence Interval of OR		p-value
Group				
<i>Comparison group</i>	1.00	(ref)		
<i>QI group</i>	0.77	0.38	1.59	0.485
Time				
<i>Initial observation</i>	1.00	(ref)		
<i>Final observation</i>	1.00			
Interaction				
<i>Group*Time</i>	19.12	11.53	31.72	<0.001
Gender				
<i>Female</i>	1.00	(ref)		
<i>Male</i>	1.24	0.68	2.27	0.479
Age				
<i><=34</i>	1.00	(ref)		
<i>35-44</i>	0.65	0.26	1.61	0.353
<i>45-54</i>	0.87	0.39	1.95	0.739
<i>55-64</i>	1.18	0.50	2.82	0.703
<i>>=65</i>	17.64	5.51	56.48	<0.001
Insurance				
<i>Private</i>	1.00	(ref)		
<i>Public (Medicare or Medicaid)</i>	1.34	0.44	4.08	0.604
<i>County program</i>	1.58	0.55	4.53	0.393
<i>Uninsured</i>	0.34	0.08	1.43	0.141
Count of prior office-based contacts (all provider specialties)				
<i>0-3 visits</i>	1.00	(ref)		
<i>4-8 visits</i>	0.86	0.39	1.91	0.718
<i>9-14 visits</i>	1.16	0.51	2.67	0.720
<i>>=15 visits</i>	1.78	0.71	4.45	0.216
Visit type at project initiation				
<i>Initial</i>	1.00	(ref)		
<i>Follow-up</i>	1.01	0.49	2.10	0.979
Number of risk factors other than medication(s) and age^a				
<i>Count variable</i>	1.46	1.03	2.08	0.034

^a Includes heart disease (congestive heart failure or coronary artery disease), diabetes, lung disease (chronic obstructive pulmonary disease or asthma), chronic renal failure, or being a current smoker. Possible range 0-5, actual range 0-4.

in vaccine coverage and many individuals at risk for preventable health loss¹²⁻¹⁵. We implemented a QI project incorporating patient education with the opportunity for immediate immunization for patients prescribed new or existing immunosuppressive therapies in a specialty care clinic. We found 81% (105 of 129) of patients with incomplete pneumococcal immunization accepted immediate vaccination. These data demonstrate that immunization coverage in patients on immunosuppressive medications can be markedly improved by direct physician recommendation with convenient, immediate availability of the pneumococcal vaccine during specialty care.

The ACIP guidelines for pneumococcal immunization are complex. There are two nonequivalent pneumococcal vaccines, PCV-13 and PPSV23 with indications by age, specific illnesses, lifestyle behaviors, sequence of administration, and broad categories of risk including immunocompromise³⁵. Recommendations are for single and in other scenarios for both vaccines. In circumstances where both vaccines are recommended, a specific sequence is recommended, with PCV-13 initially then PPSV23 given 8 weeks later. Patients in the QI program were likely immunized for other indications. We found patients were more likely to be vaccinated if they were over 65 or had other indications for pneumococcal immunization (Table 4). The EMR system of both institutions has an automatic care-gap function to remind clinicians of recommended practices compared to current care. Currently, both sites include age 65 or older as the only trigger for care-gap pneumococcal immunization reminder. The EMR was therefore an immunization barrier at both institutions. Improved EMR programming could improve reminders for pneumococcal

immunizations, improve care-gap recognition, and potentially improve immunization uptake.

Table 5. Results of logistic regression model examining adjusted associations between receipt of one or more pneumonia vaccinations during the QI project and patient characteristics. Includes persons in the QI group who were not already fully immunized at initial observation (n=129).

	Odds Ratio (OR)	95% Confidence Interval of OR	p-value
Gender			
Female	1.00	(ref)	
Male	1.06	0.35 3.24	0.917
Age			
<=34	1.00	(ref)	
35-44	0.81	0.20 3.37	0.777
45-54	3.79	0.56 25.67	0.172
55-64	1.40	0.26 7.64	0.699
>=65	1.06	0.15 7.50	0.955
Insurance			
Private	1.00	(ref)	
Public (Medicare or Medicaid)	0.89	0.15 5.22	0.893
County program	1.10	0.15 8.06	0.927
Uninsured	0.07	0.01 0.59	0.015
Patient Used Translator			
Yes	1.00	(ref)	
No	7.14	0.91 56.31	0.062
Count of prior office-based contacts (all provider specialties)			
0-3 visits	1.00	(ref)	
4-8 visits	0.62	0.17 2.28	0.473
9-14 visits	0.85	0.20 3.68	0.829
>=15 visits	0.74	0.14 3.82	0.717
Visit type at project initiation			
Initial	1.00	(ref)	
Follow-up	1.98	0.52 7.51	0.317
Number of indications other than medication(s) and age^a			
Count variable	0.98	0.50 1.91	0.952
Immunosuppressive medications used prior to initial observation			
No	1.00	(ref)	
Yes	0.40	0.08 2.06	0.271

^a Includes heart disease (congestive heart failure or coronary artery disease), diabetes, lung disease (chronic obstructive pulmonary disease or asthma), chronic renal failure, or being a current smoker. Possible range 0-5, actual range 0-4

Other systematic barriers to optimal immunization include ambiguity around who is responsible for vaccination. Patients with multiple specialty healthcare system contacts may have fewer primary care immunization opportunities³⁶. The official position of the ACIP is that every healthcare provider has a fundamental responsibility for ensuring patients are current with immunizations. The National Psoriasis Foundation recommends that dermatologists give immunization education but vaccination should be by primary care clinicians²³. Another systems barrier is incomplete communication between multiple providers. Patients, especially those with chronic health problems, may require care from multiple specialists as well as primary care providers, and a patient's immunization history can be uncertain, inaccurate, or imperfectly shared between these locations^{36,37}.

We evaluated such barriers in our local context. Since every clinician could act as a potential immunizer, we sought to identify whether the frequency and type of outpatient visits over time impacted immunization status at first observation. We identified office-based visits with primary, dermatological, and other specialty providers for all patients during the 12 months prior to first observation. We found that the number of prior office visits was not significantly associated with immunization level after controlling for other factors (Table 4). This demonstrates "diffusion of responsibility" or a situation where if everyone is responsible for immunizations, no one is responsible. One solution would be for the ACIP to define which provider is responsible for certain immunizations more precisely. The indication for immunization could direct consensus to standardize accountability. In this regard, the provider created indications could be managed by the prescribing provider. At the same time,

Table 6. Association between immunization status at initial observation and prior immunosuppressive use.

Immunization Status at Initial Observation	Total n=201 % (95% CI)	Used immunosuppressive medications prior to initial observation % (95% CI)			Time on immunosuppressive medications prior to initial observation % (95% CI)					
		No n=34	Yes n=167	p-value	None: New User n=34	<1 Year n=36	1 to <3 years n=48	3 to <6 years n=33	≥6 years n=50	p-value
No immunization	67.2 (60.3, 73.4)	70.6 (53.0, 83.6)	66.5 (58.9, 73.3)	0.725	70.6 (53.0, 83.6)	77.8 (61.1, 88.6)	70.8 (56.3, 82.1)	57.6 (40.1, 73.3)	60.0 (45.8, 72.7)	0.119
Partially immunized	22.4 (17.1, 28.7)	17.6 (8.0, 34.5)	23.3 (17.5, 30.4)		17.6 (8.0, 34.5)	8.3 (2.6, 23.3)	25.0 (14.6, 39.3)	30.3 (16.9, 48.1)	28.0 (17.2, 42.1)	
Fully immunized	10.5 (6.9, 15.5)	11.8 (4.4, 27.9)	10.2 (6.4, 15.8)		11.8 (4.4, 27.9)	13.9 (5.8, 29.7)	4.2 (1.0, 15.5)	12.1 (4.5, 28.6)	12.0 (5.4, 24.5)	

routine immunizations may be best done by primary care clinicians.

The cost of care affects adherence to health care immunization recommendations^{38,39}. A 2012 National Health Interview Survey showed pneumococcal coverage of adults at high-risk for pneumococcal pneumonia was 9.8% versus 23.0% in underinsured patients vs. insured patients⁴⁰. In our QI project, we also identified cost as a barrier to immunization. Uninsured patients were the only group in which the QI intervention was not successful (unadjusted p=0.007, adjusted p=0.015; Table 5). In pediatric populations, the Vaccine For Children program covers vaccine costs for children unable to pay⁴¹. A similar public program for adults could reduce vaccine disparities and increase uninsured patients' opportunities to be immunized.

Immunosuppression attenuates the immunological response to vaccination, and ideally, patients complete their immunizations before starting immunosuppressive therapies⁴². In this QI project where immunizations were immediately available as part of the process of initiating immunosuppressive treatment, 75% of those in the QI group (18/24; 95% CI: 53.0, 88.9) and 0% in the comparison group (0/10) received at least one

pneumococcal vaccination before starting immunosuppression. Our results suggest that one potential method to improve immunization coverage of patients preparing to initiate immunosuppressive medications would be to have immunizations immediately available for administration as part of the immunosuppressant preparation process.

There have been mixed results from quality improvement and other initiatives to increase immunization coverage⁴³⁻⁴⁷. Ineffective strategies included patient education by nursing, point-of-care paper worksheets with questionnaires, and letters to patients³¹. Successful strategies have included designating non-physician staff responsible for vaccine administration, designated clinics for preventive care, standing orders, and email reminders or prompts to providers^{29,30,48-50}. The most effective strategies have been system-level interventions. These included electronic reminders with linked order sets, physician auditing and feedback, patient outreach, and printed prescriptions. Prior research examining the impact of these strategies found that the receipt rate for any pneumococcal immunization increased 160%, from roughly 29% to 46%⁴⁹. Our QI approach of physician recommendation with convenient, immediate availability of the

pneumococcal vaccine during specialty care had 1.5 times this impact -- the predicted probability for an immune suppressed patient to have received one or more immunizations against pneumococcal pneumonia rose 247% in the presence of our intervention, from 34% to 84%. Given our experience it is likely this method could improve care if it were adopted by others.

There are several limitations to our analyses. First, our data are geographically and demographically narrow, representing the experience of two dermatology practices in north-central Texas primarily serving patient populations eligible for subsidized medical care. Our patient population may therefore not represent the overall patient population on immunosuppressive medications. Second, the study was retrospective in design, and data may have been missed or not collected. This may impact some areas of the study's power. Third, although patients from two clinics were included in analyses, small sample sizes precluded us from statistically adjusting for the multi-site nature of the data⁵¹. Larger sample sizes of patients seen in a greater number of specialty practices by a larger number of clinicians are needed to replicate our findings and solidify intervention effect estimates. We analyzed the combined effect of physician recommendation, patient education, and the immediate availability of immunizations. As a result, we cannot determine the extent to which each intervention resulted in increased vaccine uptake.

CONCLUSION

We observed, then successfully addressed, a substantial gap between recommended pneumococcal immunization in immunosuppressed patients and actual

immunization coverage among adult patients receiving specialist dermatology care. A dual strategy of direct patient education by the treating physician with immediate availability of vaccine and administration resulted in 81% of these high-risk patients obtaining full or partial pneumococcal immunization, a 247% increase in the predicted probability of full or partial immunity over baseline. Wider adoption of this model and its adaptation to other immunizations and settings is an important opportunity to reduce vaccine-preventable illness, including COVID-19, and improve population health.

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References:

1. Zabana Y, Rodríguez L, Lobatón T, et al. Relevant Infections in Inflammatory Bowel Disease, and Their Relationship With Immunosuppressive Therapy and Their Effects on Disease Mortality. *Journal of Crohn's and Colitis*. 2019;13(7):828-837.
2. Toruner M, Loftus EV, Harmsen WS, et al. Risk Factors for Opportunistic Infections in Patients With Inflammatory Bowel Disease. *Gastroenterology*. 2008;134(4):929-936.
3. Radovits BJ, Fransen J, Al Shamma S, Eijsbouts AM, van Riel PLCM, Laan RFJM. Excess mortality emerges after 10 years in an inception

- cohort of early rheumatoid arthritis. *Arthritis Care & Research*. 2010;62(3):362-370.
4. Cobb S, Anderson F, Bauer W. Length of Life and Cause of Death in Rheumatoid Arthritis. *New England Journal of Medicine*. 1953;249(14):553-556.
 5. Abuabara K, Azfar RS, Shin DB, Neimann AL, Troxel AB, Gelfand JM. Cause-specific mortality in patients with severe psoriasis: a population-based cohort study in the U.K. *Br J Dermatol*. 2010;163(3):586-592.
 6. Doran MF, Crowson CS, Pond GR, O'Fallon WM, Gabriel SE. Frequency of infection in patients with rheumatoid arthritis compared with controls: A population-based study. *Arthritis & Rheumatism*. 2002;46(9):2287-2293.
 7. Jit M. The risk of sequelae due to pneumococcal meningitis in high-income countries: A systematic review and meta-analysis. *Journal of Infection*. 2010;61(2):114-124.
 8. Glück T, Müller-Ladner U. Vaccination in Patients with Chronic Rheumatic or Autoimmune Diseases. *Clinical Infectious Diseases*. 2008;46(9):1459-1465.
 9. van Aalst M, Lötsch F, Spijker R, et al. Incidence of invasive pneumococcal disease in immunocompromised patients: A systematic review and meta-analysis. *Travel Medicine and Infectious Disease*. 2018;24:89-100.
 10. Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host. *Clinical Infectious Diseases*. 2013;58(3):e44-e100.
 11. Lopez A, Mariette X, Bachelez H, et al. Vaccination recommendations for the adult immunosuppressed patient: A systematic review and comprehensive field synopsis. *Journal of Autoimmunity*. 2017;80:10-27.
 12. Haroon M, Adeeb F, Eltahir A, Harney S. The uptake of influenza and pneumococcal vaccination among immunocompromised patients attending rheumatology outpatient clinics. *Joint Bone Spine*. 2011;78(4):374-377.
 13. Hmamouchi I, Winthrop K, Launay O, Dougados M. Low rate of influenza and pneumococcal vaccine coverage in rheumatoid arthritis: Data from the international COMORA cohort. *Vaccine*. 2015;33(12):1446-1452.
 14. Loubet P, Verger P, Abitbol V, Peyrin-Biroulet L, Launay O. Pneumococcal and influenza vaccine uptake in adults with inflammatory bowel disease in France: Results from a web-based study. *Digestive and Liver Disease*. 2018;50(6):563-567.
 15. Curtis JR, Arora T, Narongroeknawin P, et al. The delivery of evidence-based preventive care for older Americans with arthritis. *Arthritis Res Ther*. 2010;12(4):R144-R144.
 16. Bellucci E, Terenzi R, La Paglia G, et al. One year in review 2016: pathogenesis of rheumatoid arthritis. *Clin Exp Rheumatol*. 2016;34(5):793-801.
 17. Subesinghe S, Rutherford AI, Ibrahim F, Harris H, Galloway J. A large two-centre study in to rates of influenza and pneumococcal vaccination and infection burden in rheumatoid arthritis in the UK. *BMC musculoskeletal disorders*. 2016;17(1):322.
 18. Johnson DR, Nichol KL, Lipczynski K. Barriers to Adult Immunization. *The American Journal of Medicine*. 2008;121(7, Supplement 2):S28-S35.
 19. Loubet P, Kernéis S, Groh M, et al. Attitude, knowledge and factors associated with influenza and pneumococcal vaccine uptake in a large cohort of patients with secondary immune deficiency. *Vaccine*. 2015;33(31):3703-3708.
 20. Lawson EF, Trupin L, Yelin EH, Yazdany J. Reasons for failure to receive pneumococcal and influenza vaccinations among immunosuppressed patients with systemic lupus erythematosus. *Seminars in Arthritis and Rheumatism*. 2015;44(6):666-671.
 21. Doe S, Pathare S, Kelly CA, Heycock CR, Binding J, Hamilton J. Uptake of influenza vaccination in patients on immunosuppressant agents for rheumatological diseases: a follow-up audit of the influence of secondary care. *Rheumatology*. 2007;46(4):715-716.
 22. Lanternier F, Henegar C, Mouthon L, Blanche P, Guillevin L, Launay O. Low influenza-vaccination rate among adults receiving immunosuppressive therapy for systemic inflammatory disease. *Annals of the Rheumatic Diseases*. 2008;67(7):1047.
 23. Wine-Lee L, Keller SC, Wilck MB, Gluckman SJ, Van Voorhees AS. From the Medical Board of the National Psoriasis Foundation: Vaccination in adult patients on systemic therapy for psoriasis. *Journal of the American Academy of Dermatology*. 2013;69(6):1003-1013.
 24. Furer V, Rondaan C, Heijstek MW, et al. 2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. *Annals of the Rheumatic Diseases*. 2020;79(1):39.
 25. Wong PKK, Hanrahan P. Management of vaccination in rheumatic disease. *Best Practice & Research Clinical Rheumatology*. 2018;32(6):720-734.
 26. Lejri-Ei Euchti H, Chirpaz E, Foucher A, et al. Vaccination against influenza and pneumococcal infections in patients with autoimmune disorders

- under biological therapy: Coverage and attitudes in patients and physicians. *European Journal of Internal Medicine*. 2019;69:25-31.
27. McCarthy EM, Azeez MA, Fitzpatrick FM, Donnelly S. Knowledge, Attitudes, and Clinical Practice of Rheumatologists in Vaccination of the At-Risk Rheumatology Patient Population. *JCR: Journal of Clinical Rheumatology*. 2012;18(5).
 28. Centers for Disease C. Pneumococcal ACIP Vaccine Recommendations. Published November 21, 2014. Accessed October 9, 2020.
 29. Szilagyi P, Vann J, Bordley C, et al. Interventions aimed at improving immunization rates. *Cochrane Database Syst Rev*. 2002(4):Cd003941.
 30. Stone EG, Morton SC, Hulscher ME, et al. Interventions That Increase Use of Adult Immunization and Cancer Screening Services. *Annals of Internal Medicine*. 2002;136(9):641-651.
 31. Murray K, Low C, O'Rourke A, et al. A quality improvement intervention failed to significantly increase pneumococcal and influenza vaccination rates in immunosuppressed inflammatory arthritis patients. *Clinical Rheumatology*. 2020;39(3):747-754.
 32. Ventola CL. Immunization in the United States: Recommendations, Barriers, and Measures to Improve Compliance: Part 1: Childhood Vaccinations. *P T*. 2016;41(7):426-436.
 33. Reeves BC, Wells GA, Waddington H. Quasi-experimental study designs series-paper 5: a checklist for classifying studies evaluating the effects on health interventions-a taxonomy without labels. *J Clin Epidemiol*. 2017;89:30-42.
 34. Burea USC. U.S. Census Bureau QuickFacts: Tarrant County, Texas. <https://www.census.gov/quickfacts/tarrantcountytexas>. Published 2010. Accessed.
 35. Green C, Moore C, Mahajan A, Bajaj K. A simple approach to pneumococcal vaccination in adults. *Journal of Global Infectious Diseases*. 2018;10(3):159-162.
 36. Doherty M, Schmidt-Ott R, Santos JI, et al. Vaccination of special populations: Protecting the vulnerable. *Vaccine*. 2016;34(52):6681-6690.
 37. Dorell CG, Jain N, Yankey D. Validity of parent-reported vaccination status for adolescents aged 13-17 years: National Immunization Survey-Teen, 2008. *Public Health Rep*. 2011;126 Suppl 2(Suppl 2):60-69.
 38. Hinman AR, Orenstein WA. Adult Immunization: What Can We Learn from the Childhood Immunization Program? *Clinical Infectious Diseases*. 2007;44(12):1532-1535.
 39. National Vaccine Advisory C. Recommendations from the National Vaccine Advisory committee: standards for adult immunization practice. *Public Health Rep*. 2014;129(2):115-123.
 40. Lu P-j, O'Halloran A, Williams WW. Impact of Health Insurance Status on Vaccination Coverage Among Adult Populations. *American Journal of Preventive Medicine*. 2015;48(6):647-661.
 41. Whitney CG, Zhou F, Singleton J, Schuchat A, Centers for Disease C, Prevention. Benefits from immunization during the vaccines for children program era - United States, 1994-2013. *MMWR Morb Mortal Wkly Rep*. 2014;63(16):352-355.
 42. Agarwal N, Ollington K, Kaneshiro M, Frenck R, Melmed GY. Are immunosuppressive medications associated with decreased responses to routine immunizations? A systematic review. *Vaccine*. 2012;30(8):1413-1424.
 43. Shea S, DuMouchel W, Bahamonde L. A meta-analysis of 16 randomized controlled trials to evaluate computer-based clinical reminder systems for preventive care in the ambulatory setting. *J Am Med Inform Assoc*. 1996;3(6):399-409.
 44. Vann JCJ, Jacobson RM, Coyne-Beasley T, Asafu-Adjei JK, Szilagyi PG. Patient reminder and recall interventions to improve immunization rates. *Cochrane Database of Systematic Reviews*. 2018(1).
 45. Dexter PR, Perkins SM, Maharry KS, Jones K, McDonald CJ. Inpatient computer-based standing orders vs physician reminders to increase influenza and pneumococcal vaccination rates: a randomized trial. *Jama*. 2004;292(19):2366-2371.
 46. Nichol KL. Ten-year durability and success of an organized program to increase influenza and pneumococcal vaccination rates among high-risk adults. *The American journal of medicine*. 1998;105(5):385-392.
 47. Briss PA, Rodewald LE, Hinman AR, et al. Reviews of evidence regarding interventions to improve vaccination coverage in children, adolescents, and adults¹The names and affiliations of the Task Force members are listed on page v of this supplement and at <http://www.thecommunityguide.org22>Some of this material was published previously in: Shefer A, Briss P, Rodewald L, et al. Improving immunization coverage rates: an evidence-based review of the literature. *Epidemiol Rev* 1999;20:96-142. *American Journal of Preventive Medicine*. 2000;18(1, Supplement 1):97-140.
 48. Desai SP, Lu B, Szent-Gyorgyi LE, et al. Increasing pneumococcal vaccination for

- immunosuppressed patients: A cluster quality improvement trial. *Arthritis & Rheumatism*. 2013;65(1):39-47.
49. Baker DW, Brown T, Lee JY, et al. A Multifaceted Intervention to Improve Influenza, Pneumococcal, and Herpes Zoster Vaccination among Patients with Rheumatoid Arthritis. *J Rheumatol*. 2016;43(6):1030-1037.
50. Dempsey AF, Zimet GD. Interventions to Improve Adolescent Vaccination: What May Work and What Still Needs to Be Tested. *American Journal of Preventive Medicine*. 2015;49(6, Supplement 4):S445-S454.
51. Feaster DJ, Mikulich-Gilbertson S, Brincks AM. Modeling site effects in the design and analysis of multi-site trials. *Am J Drug Alcohol Abuse*. 2011;37(5):383-391.