IMPROVING VACCINATION FOR YOUNG CHILDREN (IVY): A STEPPED-WEDGE CLUSTER RANDOMIZED TRIAL

ABSTRACT

Purpose & Scope: Routine childhood vaccination is a powerful tool to reduce morbidity and mortality. However, vaccination rates in the U.S. remain below goals. Strong recommendations from healthcare providers have been shown to positively impact vaccination decisions, thus communication from these stakeholders is critical. We sought to improve vaccination rates for Tennessee children at 2 years of age through the development and implementation of a new educational and quality improvement program, Improving Vaccination for Young Children (IVY).

Methods: Eight practices were recruited and randomized to receive the IVY intervention over a 13-month study period within a stepped-wedge cluster randomized trial (SWCRT). Educational and quality improvement (QI) components were developed for providers and clinical staff. Practices selected at least 2 interventions to incorporate. Vaccination status (yes/no) data by vaccine dose was collected from electronic medical records. Data was aggregated and summarized monthly for each practice. The primary outcome was receipt of all vaccinations (binary, yes/no) for children turning 2 years of age. The Hussey and Hughes model-based approach for analyzing data from a cross-sectional SW-CRT was used to analyze binary outcomes.

Results: Overall observed vaccination rates indicated no significant difference in the periods before and after rollout of the intervention (58.3% vs. 57.0%, respectively; p=0.4). However, secondary outcome analysis of Combination 10 vaccination rates without influenza using a chi-square test indicated a significant difference in the rates before and after rollout (70.4% versus 74.4%, respectively; p=0.004).

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PURPOSE AND BACKGROUND

Routine childhood vaccination is a powerful tool to reduce morbidity and mortality. The reasons for declining vaccination coverage rates in children are numerous and varied. It is well known that parental concerns about the safety or necessity of vaccines impact vaccine acceptance. Strong recommendations from healthcare providers have been shown to positively impact vaccination decisions, however, earlier work demonstrated that vaccine education for healthcare providers during residency was lacking. Furthermore, some providers and their staff believe that certain vaccines are unnecessary or unsafe, making these individuals less likely to strongly support routine vaccinations for children. Earlier work found that pediatric healthcare providers may not receive adequate education in residency to address parental vaccine concerns and that clinical staff may have concerning attitudes or beliefs regarding vaccines. Other studies have shown that providers desire additional knowledge and skills to discuss vaccines with patients and families. Given that undervaccination due to any reason increases the risk of acquiring vaccine preventable diseases, it is imperative for pediatric providers and all clinical team members to fully understand and communicate the safety and importance for all recommended childhood vaccines.

To address this need, we developed and implemented a new program, Improving Vaccination for Young Children (IVY). IVY incorporates vaccine-focused education for pediatric providers and pediatric office staff in addition to evidence-based quality improvement initiatives. We hypothesized that implementation of IVY would improve Combination 10 vaccination rates for Tennessee children at 2 years of age.
The purpose of this study is to assess the effectiveness of the IVY program for improving monthly clinic vaccination rates for 24-month-old children within the context of a stepped wedge cluster randomized trial (SW-CRT). This study tested the hypothesis that monthly clinic vaccination rates would be significantly higher after implementation of the IVY program (intervention) than before (control). Secondary analyses tested for delayed effects related to the Quality Improvement (QI) and Booster components of the program, and exploratory analyses tested for differential effects between clinics and between clinic types (i.e., academic or community).

**METHODS**

**Setting and Participants**

This project was developed and implemented from February 2019 through February 2020 in middle Tennessee, United States. Eight pediatric practices were recruited to include a diverse population of both urban and rural settings. Targeted participants within recruited practices were practicing pediatric care providers and clinical staff (nurses, medical assistants (MAs)).

Three practices affiliated with Vanderbilt University Medical Center (VUMC) participated. VUMC practice sites care for children from a variety of payers and are representative of diverse socioeconomic groups. Two sites have patient populations primarily insured through Tennessee Medicaid affiliated plans, while one practice’s patient population is primarily privately insured.

Private practices were recruited from the largest network for private pediatric practices in the state, the Cumberland Pediatric Foundation (CPF). CPF’s primary care practice members are located across urban, suburban, and rural settings, with a geographical range stretching across...
40 counties in Tennessee. Five practices were recruited across settings (urban, suburban, and rural).

Two types of participant incentives were implemented. For clinical staff and non-medical doctor providers, monetary gift cards were given for completion of educational modules. For medical doctors, providers who completed educational modules and whose practice met the Quality Improvement requirements were eligible to receive MOC4 credit.

**Intervention**

The Community Preventive Services Task Force (CPSTF), established by the U.S. Department of Health and Human Services to develop guidance on community health promotion and disease prevention, conducted a systematic review to evaluate effective measures to improve vaccination rates in targeted populations. Evidence from this review supports that incorporating multiple interventions within a health care system has the greatest success in positively impacting vaccination rates. The IVY program incorporates multiple interventions with options to select appropriate QI interventions by practice sites in accordance with these findings. Details of the development of the IVY program are described below.

Two modules were developed for each group (providers and clinical staff): a primary educational module (Module 1) and a “booster” module (Booster). Modules included robust key educational information for each group (i.e., modules were different assuming a higher baseline level of immunization knowledge among providers). Topics included were identified through the Phase I Chapter Quality Network (CQN) Immunization Project of the American Academy of Pediatrics, expert input from three additional vaccine experts, and literature review. The Booster module also included select educational material yet focused more specifically on influenza vaccine and communication techniques. The modules will be developed using the e-Learning Williams, SE. IVY Final Report
software Articulate RISE\textsuperscript{22}. Module content and design were developed using the Kolb framework\textsuperscript{23} and best practices from Cognitive Load theory\textsuperscript{24} and multimedia learning\textsuperscript{25}. Modules were pilot tested with volunteer staff at VUMC prior to implementation and revised as needed.

A QI coaching session was designed utilizing the Model for Improvement and the 4Pillars™ Practice Transformation Program format. 4Pillars™ was designed specifically to assist adult healthcare providers protect their patients from vaccine preventable diseases through QI initiatives.\textsuperscript{26, 27} The program has, however, been successful in improving childhood influenza vaccination rates\textsuperscript{28, 29} and reducing racial disparities associated with influenza vaccination among children with asthma.\textsuperscript{30} Specific QI options to improve vaccination uptake for patients less than 2 years of age were included and provided to practices. Included options were identified from both the 4Pillars™ program and the CQN Immunizations Project. The QI coaching session also introduced the Model for Improvement as a QI framework\textsuperscript{31} to assist in determination of goals for practices and the selection of QI changes for each practice to reach their goals.

Both modules were housed on the CPF website with password protected access. Participants were provided a unique login and password to access modules. Module 1 was provided to all participants through a direct email in addition to recommendation to practice leadership to encourage completion. Two follow up emails were sent to maximize completion over the course of one month. The in-person QI coaching session was then implemented approximately one month after the introduction of Module 1. The QI coaching session was led by Dr. Williams and a CPF assigned QI Coach. Upon completion of the QI session, practices selected change option(s) to implement within 2 weeks following the session. Practices selected at least two
change options. Dr. Williams and the QI Coach were available to provide assistance in designing and implementing the intervention for the practice if needed. The Booster module was provided in a similar manner approximately 2 months after the QI coaching session. This delay allowed for the Booster to surround the start of influenza vaccine season with the intention of maximizing influenza vaccine uptake.

Study Design
The IVY study includes three phases: 1) development of the project components, 2) implementation of components, and 3) ongoing and end-of-study measurement of project impact on childhood vaccination rates within the modern SW-RCT design.32 Eight practices (clusters) were randomized to receive the IVY intervention over a 13-month study period (Feb 19 – Feb 20). Patients are clustered within practices, and outcomes were assessed on cross-sectional samples of individuals at each practice at 13 discrete, monthly time points. A baseline block of two months was also included where all practices were in the control group (Figure 1). Following this, two practices were the first to receive the intervention (Group 1). Two months after initiation of IVY in Group 1, the two practice in Group 2 received the intervention in Group 2. This was continued for 4 total Groups. There was a five-month block after implementing IVY in all practices where data was collected. Continuing to collect data in this allowed for exploration of potential effects relating to delivery of QI or the Booster module after the initial Module 1. Due to the nature of the intervention, blinding of the centers was not possible.
Outcomes

The primary outcome was Combination 10 (Combo 10) vaccination status (binary, up to date vs. not up to date) for children who turned 24 months old in the preceding month. At participating clinics, combination 10 immunization requires all doses of 10 different vaccines: four diphtheria, tetanus, pertussis (DTaP); three inactive polio (IPV); one measles, mumps, rubella (MMR); three Haemophilus influenzae type B (HiB); three hepatitis B (HepB); one varicella (Var); one hepatitis A (HepA); four pneumococcal (PCV); two-three rotavirus (Rota); and two influenza (Flu). Combo 10 status was measured at the individual child level for all eligible children within each clinic every month for 14 months. Combo 10 excluding influenza vaccination was collected and analyzed in the same manner as a secondary outcome.

Data collection
All vaccination status (yes/no) data by vaccine dose was collected and stored at the individual patient level, although it will be possible to aggregate and summarize monthly and total vaccination rates at each practice. To protect patient confidentiality, we did not have access to identifiable patient-level data, including potential covariates of interest (e.g., sex, socio-economic status, parent education level, etc.). Eligible children included patients who were seen at the participating practice at least once prior to 90 days of life. Combo 10 vaccine data is already collected monthly at all VPPCP sites. For CPF recruited practices, we utilized a data collection service, Visualize Health, to interface with EHR systems and extract vaccine data in real-time. Aggregated de-identified data from all 8 practice sites was shared with stakeholders monthly (individual practice data to practice leadership, all aggregated data shared with grantor).

**Statistical Methods**

The prespecified primary analysis employed a multilevel mixed-effects logistic regression model as an extension of the Hussey and Hughes approach for analyzing an intervention’s effect on binary outcome data from a cross-sectional SW-CRT.\textsuperscript{34} Importantly, this approach adjusts for secular trends which is critical to avoid bias from the inherent confounding of intervention effect with time in a SW-CRT design (e.g., outcome changes due to external or seasonal forces over time).\textsuperscript{35} The primary analysis used the implementation design matrix specified in the planned schedule for intervention rollout (See Figure 1). Secondary analyses tested for potential delayed intervention effects related to the QI and Booster components of the program by shifting the design matrix to correspond with the scheduled rollout of each respective component. Exploratory analyses used newer, less-well-validated, flexible extensions of the Hussey and Hughes approach to accommodate potential deviations from the underlying assumptions. Specifically, models that allowed for varying intervention effects across clusters.
(clinics), cluster groups (clinic types), and over time were employed. Intervention effects are reported as odds ratio (OR) regression coefficients with 95% confidence intervals (CIs), and model-estimated vaccination rates are presented graphically to facilitate interpretation. Run charts and tables of the observed monthly vaccination rates at each clinic. Analyses were conducted in Stata version 15.1 (StataCorp), and statistical significance was defined with a two-sided test with $\alpha=0.05$.

**Power and Sample Size**

Power analyses were conducted to ensure that meaningful intervention effects can be detected with at least 80% power, even with conservative assumptions for important parameters, such as cell size (i.e., the number of eligible patients visiting each practice per month). Power analyses were conducted using the “steppedwedge” Stata command (Stata 14.2), which takes into account important design features of the SW-CRT methodology that can potentially affect power. Preliminary data from four VPPCP sites was used to inform estimates of the expected average baseline center vaccination rate (65%). Intracluster correlation coefficient (ICC) is expected to be small, but a variety of values were used to examine its potential effects on power (ICC range 0.01-0.05). All analyses assumed a two-tailed significance level of $\alpha=0.05$. The study has 80% power to detect a 10-point rate difference if an average of 23 eligible participants per month visit each center throughout the study.

**Ethics**

This protocol and any specific modifications were reviewed and approved by the IRB at VUMC. We requested a Waiver of Informed Consent Documentation due to the minimal risk nature of the study.
RESULTS

One patient population target included 2392 total patients seen across 8 clinics over 13 months.

Among the eight clinics, 4041 (1788 control and 2253 intervention) met inclusion criteria for our analysis over the 14-month study period [i.e., eligible patients who were seen in one of the eight participating clinics at least once prior to 90 days of life and were between 24 and 25 months of age for analysis (2 years old)].

A chi-square test of the overall observed Combo 10 vaccination rates (not adjusting for trends over time or repeated measurement within clinics) indicated that they were not significantly different in the periods before and after rollout of the intervention (58.3% versus 57.0%, respectively; p=0.4). The prespecified primary analysis (a multilevel mixed-effects logistic regression model, adjusting for trends over time and allowing a random effect for clinic) was unable to detect a statistically significant intervention effect on vaccination rate (OR=1.01; 95% CI [0.76, 1.34]; p>0.9). However, secondary outcome analysis of Combo 10 vaccination rates without influenza using a chi-square test indicated a significant difference in the rates before and after rollout (70.4% versus 74.4%, respectively; p=0.004).

Discussion

IVY was successfully developed and implemented in eight pediatric practices with varied populations and sizes. Although improvement of overall Combination 10 vaccine rates was not significant before and after initiation of the program, analysis did show significant improvement in vaccination rates when influenza vaccine was excluded.
IVY was developed using well recognized frameworks in both education and quality improvement. The positive qualitative feedback investigators received regarding the educational modules supported the successful application of effective multimedia learning practices. Further, given that practice capabilities and operations vary greatly, IVY allows for practices to select options for QI change that are most relevant, so they are able to implement choices that are feasible and achievable. We believe these are strengths to the program that helped support the success.

The study does have some limitations. The electronic health record system used varies between clinics and especially between different types of clinics (e.g., academic and community), possibly providing a source measurement error with respect to vaccination status. Tracking patient transitions to a different clinic and active/inactive statuses poses a challenge for clinics. This is especially salient in the young, 24-month-old age group analyzed in this study, where it can be difficult to know whether a patient is truly inactive or simply overdue for a follow-up visit. This issue likely lowered overall vaccination rates due to the overinclusion of inactive or transferred patients with low vaccination rates. If severity of this issue differed between clinics or clinic types or over time, it could also induce bias in the results, inflating or masking intervention effects. To protect patient confidentiality, we will not have access to identifiable patient-level data, including potential covariates of interest (e.g., sex, socio-economic status, parent education level, etc.). Therefore, our ability to adjust for potential important patient-level covariates is limited.
Overall, the novel program IVY was successfully developed and implemented in eight clinical practices and shows promise to improved childhood vaccine rates. Further refinement, implementation, and evaluation of this program is warranted.

REFERENCES


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