"Less Pain, Less Fuss, Right Now!" and "Make It Count!"—Multilevel Interventions for Patient, Parent, and Practice to Enhance Provider Recommendations for HPV Vaccination

Statistical Analysis Plan

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General Study Information

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Study Title: "Less Pain, Less Fuss, Right Now!" and "Make It Count!"—Multilevel Interventions for

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Statistical Analysis Plan

Power Statement: Stepped-wedge cluster randomization trials typically have more statistical power than other cluster randomized designs, because each cluster is able to serve as its own control, accounting directly for the within cluster correlation of outcomes. Because of the complex nature of the design, we estimate statistical power using simulation, which accounted for potential differences in baseline rates across sites. Based on pilot data from a 12-month period, we assumed an average cluster size of 800 children (400 males and 400 females), a baseline probability of requiring any vaccination of 25% (log-odds of -1.1), and a conservative estimate of the standard deviation of the random effect of 0.5, assuming a secular treatment effect. These estimates are conservative. We have sufficient power to detect meaningful patient-centered and provider-level effects in both the sex-stratified and full cohorts. For the interaction between patient-centered and provider-level effects (with the same assumptions described above), based on the simulation, we have at least 80% power to detect an odds ratio (OR) of 1.5 or greater when looking at males and females separately and of 1.34 or greater in the full cohort. To aid in interpretation, an OR of 1.34 means that a significant interaction would be detected if the synergistic effect of the two treatments or interventions is 1.34 times higher than the product of the individual ORs. For example, with ORs of 1.28 for both interventions individually, we can detect a synergistic effect of 2.2. Although our power estimates are conservative, power is somewhat marginal (70% to detect an OR of 1.45) for the synergistic effect in the sex-stratified cohorts; however, we have sufficient power to detect an effect using the combined sample. We conducted several sensitivity analyses adjusting the terms in our model (baseline probability, random effect standard deviation and secular trend) and found small changes in our already conservative power estimates. We used average cluster instead of actual size which was reasonable given our pilot data indicate only a slight imbalance across the clusters. Our average observed total cluster size was 895, with close to 50% male and 50% female; we assumed an average cluster size of 800 (400 for each sex) to allow for decreases in eligible participants overtime as a result of the effect of our interventions.

Data Analysis Plan: We will summarize patient characteristics (including sex, age, and race/ethnicity, by intervention status (usual care, parent reminder-recall letters, provider audit-feedback reports, and combination of parent reminder-recall letters, provider audit-feedback reports). All patients will be analyzed on an intention to treat status; this principle will be extended to the practice status, so that delays in implementation of an intervention will not affect the intervention status of patients. We will use generalized linear mixed models to assess the effects of the interventions. All models will be assessed both overall and stratified by sex in recognition of differential rates of HPV vaccination among males and females. Our main model will be a mixed effects logistic regression model which will allow us to test the three primary aims.

Endpoints

Our outcome variables are the rates of HPV-vaccine receipt for empaneled eligible males and females, measured at the end of the last day of each 12-month step. Furthermore, eligible individuals must be due for a dose of an HPV vaccine at the start of the 12-month-long step. They could be due for the first, second, or third dose. Eligibility for a dose depends on previously received valid doses received before the beginning of the 12- month-long step. Eligibility also depends upon the amount of time that passed between the last received valid dose and the start of the 12-month-long step. Valid doses include doses given at nine years or older (the minimum age permitted by the ACIP) and meet the minimum intervals. If the individual has received no valid doses previously at age 11 or 12, then the individual is eligible for a first dose. If the individual has previously received one valid dose, and at least 5 months has passed since that dose before the start of the 12-month-long step, then the individual is eligible for a second dose. If the individual has previously received two valid doses but the second dose was given less than 5 months from the first and at least 12 weeks have passed since the second dose and 24 weeks since the first dose, both before the start of the 12-month-long step, then the individual is eligible for a third dose.