Engaging clinical champions to Improve HPV Vaccination

Hypotheses and Analytic Plan
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Analysis plan for HPV vaccine champion trial

The purpose of this cluster randomized non-inferiority trial is to compare Champion Announcement Approach Training (AAT) to Traditional AAT on HPV vaccine initiation among patients ages 9-12.

Hypotheses

The primary hypothesis is that Champion AAT will be non-inferior to Traditional AAT for increasing HPV vaccine initiation. By engaging highly influential physicians, we anticipate that Champion AAT will be at least as effective as Traditional AAT for increasing HPV vaccine uptake.

Design & Power

We will randomize 40 clinics within multiple healthcare systems to the two trial arms (Champion vs Traditional AAT). To maximize balance in trial arms, we block randomization by system in a 1:1 ratio.

With 20 clinics per study arm, we will have ≥80% power to conclude non-inferiority of Champion vs Traditional AAT when Champion AAT increases HPV vaccine uptake ≥8% points over the secular trend. This calculation assumes: 1) a clinic-level ICC of .033 for change in HPV vaccine initiation, as observed in our pilot work; 2) a non-inferiority margin of .04; 3) 100 patients, ages 9-12, per clinic on average; 4) a secular trend of 10% points; and 5) Traditional AAT effect of 5% points, as observed in our prior trial.35 Achieving an effect size of ≥8% points with Champion AAT is feasible, given that we are modeling HPV vaccination among unvaccinated adolescents, whose uptake will be higher proportionally than the general population.

The non-inferiority margin, delta, will be .04, which we have selected to detect any clinically meaningful difference between the effectiveness of our interventions. To test for non-inferiority with a margin of .04, we will translate the lower and upper 95% confidence interval limits into predicted probability units and conclude that Champion AAT is inferior if the transformed upper confidence limit falls below .04.

Analytic Plan

Primary trial outcome: HPV vaccine initiation by 12-month follow-up

We will assess the vaccination status of adolescents who are HPV vaccine naïve at baseline, using routinely collected EHR data from our healthcare systems and submitted to the Wisconsin Collaborative for Healthcare Quality.

We will model HPV vaccine initiation using a generalized estimating equation (GEE) for logistic outcomes. GEE models accommodate non-independence due to nesting of patients within clinics by adjusting standard error terms. The outcome of the model will be patient-level HPV vaccine initiation at follow-up (0=no, 1=yes):

$$ln(\frac{p(vax_{2ij})}{1-p(vax_{2ij})}) = b_0 + b_1 Champion_j + b_2 System_j$$

Trial arm will be the primary fixed effect as a two-level, categorical variable (Champion AAT vs. Traditional AAT). Since we will be block randomizing on healthcare system, system membership will be added as an n-level, categorical covariate where n is the number of participating systems. Tests will be 2-tailed with α=.05 Statistical analyses will be conducted in SAS 9.4 (Cary, NC) and R 4.2.2.

Missing Data

We will use all available data in computing the primary outcome of HPV vaccine initiation by 12-month follow-up as per our intent-to-treat protocol. We will drop the clinic if no data are available (e.g., due to clinic closure).

Adjustment for covariates

We do not plan to adjust for demographic or other baseline characteristics per CONSORT recommendations (Consort, 2010).

Secondary trial outcome

The secondary trail outcome is HPV vaccination series completion (2 doses) at 12 months, which we will evaluate in the same manner as the primary outcome.