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Influenza Risk by Vaccination Method

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PHC6011 Epidemiology Methods II

4/13/2018

Influenza is a seasonal disease that in the United States presents mainly during the winter months and can potentially cause severe illness and sometimes even death. Given the significant public health burden that influenza poses, this analysis will evaluate whether there is any significant difference in the protections provided to children by the injected vaccine compared to the nasal spray known as FluMist.

Purpose

This analysis explores whether, for children in the United States during 2012, there were any significant differences in the protection against influenza provided by the injected vaccine compared to the nasal spray known as FluMist. Furthermore, the analysis evaluated whether any effect modification due to age was present.

Statistical Methods

To compare the effectiveness of the two influenza vaccine options in children, a case-control study was conducted by sampling records from the 2012 National Health Interview Survey. A univariate analysis was conducted to compare the characteristics of cases and controls. Statistical differences between cases and controls were evaluated using a Chi-square test with an alpha of 0.05.

Multivariate analysis was done by building a logistic regression model to describe the relationship between the vaccination method and the prevalence of influenza. The model was adjusted to control for sex, age, race, presence other children or elderly in the household, and indicators of long-term poor health as measured by proxy through the number of schools days missed.

To assess whether the effect of vaccination method on influenza varies by age group, an interaction term between age and vaccination method was added to the model. This analysis is presented separately.

Results

The results of the univariate analysis can be seen in **Table 1**. Cases and controls were matched on sex and age and as such, present no differences between distributions. Race was not significantly different between groups, nor was the number of individuals sharing a household with an elderly individual. Cases and controls showed a significant difference between those that reported sharing a household with other children, with controls showing a higher proportion responding *yes.* The proxy variable for poor long-term health, school days missed, was also significantly different between groups, with a higher proportion of controls reporting missing no school. The distribution of vaccination methods did not differ between groups.

Table 2 presents the odds ratios for comparing the injected vaccine to no vaccination, the nasal spray to no vaccination, and nasal spray to the injected vaccine. Both crude and adjusted odds ratios are presented. Only the crude odds ratio for injected vaccine vs. no vaccination was significant. Overall, the nasal spray appeared to be more protective than the injected vaccine both before and after adjustment; however, these results were not statistically significant at a 95% confidence level.

Table 1. Characteristics on 1680 study participants by case/control status. Numbers in parenthesis represent percentages.

	Cases (N=560)	Controls (N=1120)
Sex		
Female	276 (49.29)	552 (49.29)
Male	284 (50.71)	568 (50.71)
Age		
[0-8]	228 (40.71)	456 (40.71)
[9-17]	332 (59.29)	664 (59.29)
Race		
Black/African American only	69 (12.32)	181 (16.16)
White only	410 (73.21)	790 (70.54)
Other	81 (14.46)	149 (13.30)
Lives with other children *		
No	246 (43.93)	428 (38.21)
Yes	314 (56.07)	692 (61.79)
Lives with elderly		
No	537 (95.89)	1055 (94.2)
Yes	23 (4.11)	65 (5.8)
School days missed[a] ****		
Less than 1 week	304 (54.29)	531 (47.41)
Less than 2 weeks	83 (14.82)	74 (6.61)
2 weeks or more	57 (10.18)	41 (3.66)
None	67 (11.96)	376 (33.57)
Vaccination		
Flu shot	208 (37.14)	373 (33.3)
Nasal spray	51 (9.11)	125 (11.16)
None	301 (53.75)	622 (55.54)

[a] 49 cases and 98 controls did not provide a response.
* $p < 0.05$ for χ^2 test

Table 2. Crude and adjusted odds ratios comparing vaccination methods.

	Crude Odds Ratio 95 % CI	Adjusted Odds Ratio 95% CI
Flu shot vs None	1.247 (1.001-1.552)*	1.206 (0.957-1.52)
Nasal spray vs None	0.917 (0.643-1.308)	1.028 (0.706-1.495)
Nasal spray vs Flu shot	0.736 (0.508-1.065)	0.852 (0.578-1.255)

* $p < 0.05$ for χ^2 test

Table 3 presents the results of adding an interaction between age group and vaccination method to the model. Adjusted odds ratios comparing vaccination methods are presented for the two age stratum. Though odds ratios do appear to differ between

strata, the results showed no statistical significance. The coefficient for the interaction term in the model was not significant.

Table 3. Adjusted odds ratios per age stratum comparing vaccination methods.

	Adjusted Odds Ratios with 95% CI	
	Ages 0-8	**Ages 9-17**
Flu shot vs None	1.098 (0.743-1.624)	1.273 (0.957-1.694)
Nasal spray vs None	1.087 (0.628-1.883)	0.968 (0.581-1.615)
Nasal spray vs Flu shot	0.99 (0.559-1.754)	0.716 (0.447-1.294)

Discussion

The present analysis evaluated whether a difference existed in the protection against influenza for the injected vaccine compared to the nasal in children in the United States for 2012. Overall, there is no evidence of a superiority of one treatment versus another. However, the confidence intervals are wide indicating a large variance. Thus it would be unfair to conclude that both treatments are equally effective. Perhaps of most interest were the results obtained when comparing each vaccination option to no vaccination. The adjusted odds ratios show an elevated risk for influenza for both vaccination methods, though the results are not significant in either case.

Assessment of interaction with age did not produce any statistically significant results. However, this analysis is severely limited due to the small number of cases indicating use of nasal spray (*n=51*). This already small number will be divided when evaluating interaction leaving the analysis greatly underpowered. A further limitation of this study has to do with information bias. The data was obtained from the 2012 National Health Interview Survey and possible errors in classification cannot be dismissed. As such, the results of the analysis may present misclassification bias.

Although misclassification errors cannot be corrected in the data, the potential damaging effects can be mitigated by increasing sample size. Continuation of this analysis should include grouping survey records over several years. Assuming question and response options are standard and are asked each year, the resulting larger sample could lead to more reliable effect measures that better describe the relationship between vaccination method and prevalence of influenza. The assessment of interaction with age would also benefit from a larger sample size.