

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Monto AS, Ohmit SE, Petrie JG, et al. Comparative efficacy of inactivated and live attenuated influenza vaccines. *N Engl J Med* 2009;361:1260-7.

Comparative Efficacies of Inactivated and Live Attenuated Influenza Vaccines

WEB-based only narrative, table and two figures

Methods:

Differences in cumulative incidence proportions and confidence intervals around risk differences were calculated for compared groups. A positive lower limit of the confidence interval for risk difference was considered to indicate statistical significance.

Results:

One thousand, three hundred sixty-six surveillance specimens were collected from 970 (49.7 percent) participants from November 2007 through April 2008. Six hundred (30.7 percent) participants had one or more episodes of symptomatic illness meeting case criteria during the period of surveillance-defined study wide influenza activity (January through mid-April 2008: Figure 2). Specimens were collected on average 2.6 days after illness onset (SD=1.6, range 0 – 7 days) with no significant differences in timing of collection by intervention group.

In addition to relative risk estimates, differences in cumulative incidence proportions and confidence intervals around risk differences were calculated for compared groups and are presented in Table 4. Unlike relative risk estimates, risk differences will vary with the intensity of the outbreak. The overall pattern of risk differences is consistent to that seen with the efficacy estimates.

Seventy (3.6 percent) participants failed to complete all scheduled visits with no differential loss by vaccine/placebo group. Study analyses were conducted as intention-to-treat comparisons with all enrolled and randomized subjects included; any eligible, but unreported, illnesses experienced by subjects lost to follow-up were assumed to be non-cases since they could not be laboratory-confirmed as influenza. In order to quantify the influence of these potential lost cases on efficacy estimates, subjects without complete follow-up data were randomly assigned to case status based on the attack rate for laboratory-confirmed influenza in the placebo group (10.8%). In subsequent analyses carried out multiple times with varying subjects assigned to case status, estimates of absolute and relative efficacy varied slightly; however, in no case were the original study conclusions changed.

Table: Estimated Absolute and Relative Risk Differences of the Inactivated (TIV) and the Live-Attenuated (LAIV) Influenza Vaccines during the 2007-2008 Influenza Season in Michigan.

Laboratory-Confirmed Symptomatic Influenza	Cumulative Incidence Proportion of Influenza no. (%) of participants			Risk Differences (95% confidence interval)		
	TIV (N=813)	LAIV (N=814)	Placebo (N=325)	TIV vs. placebo	LAIV vs. placebo	TIV vs. LAIV
Culture Positive	21 (2.6%)	38 (4.7%)	31 (9.5%)	7.0% (3.6, 10.3)	4.9% (1.4, 8.4)	2.1% (0.3, 3.9)
Culture and/or Real-time PCR Positive	28 (3.4%)	56 (6.9%)	35 (10.8%)	7.3% (3.7, 10.9)	3.9% (0.1, 7.7)	3.4% (1.3, 5.6)
Culture and/or Real-time PCR Positive Influenza A	22 (2.7%)	55 (6.8%)	31 (9.5%)	6.8% (3.5, 10.2)	2.8% (-0.9, 6.4)	4.1% (2.0, 6.1)
Culture and/or Real-time PCR Positive Influenza B	6 (0.7%)	1 (0.1%)	4 (1.2%)	0.5% (-0.8, 1.8)	1.1% (-0.1, 2.3)	0.6% (0.0, 1.3)

Figure 1. Enrollment and Follow-up of Study Participants during the 2007-2008 Influenza Season in Michigan.

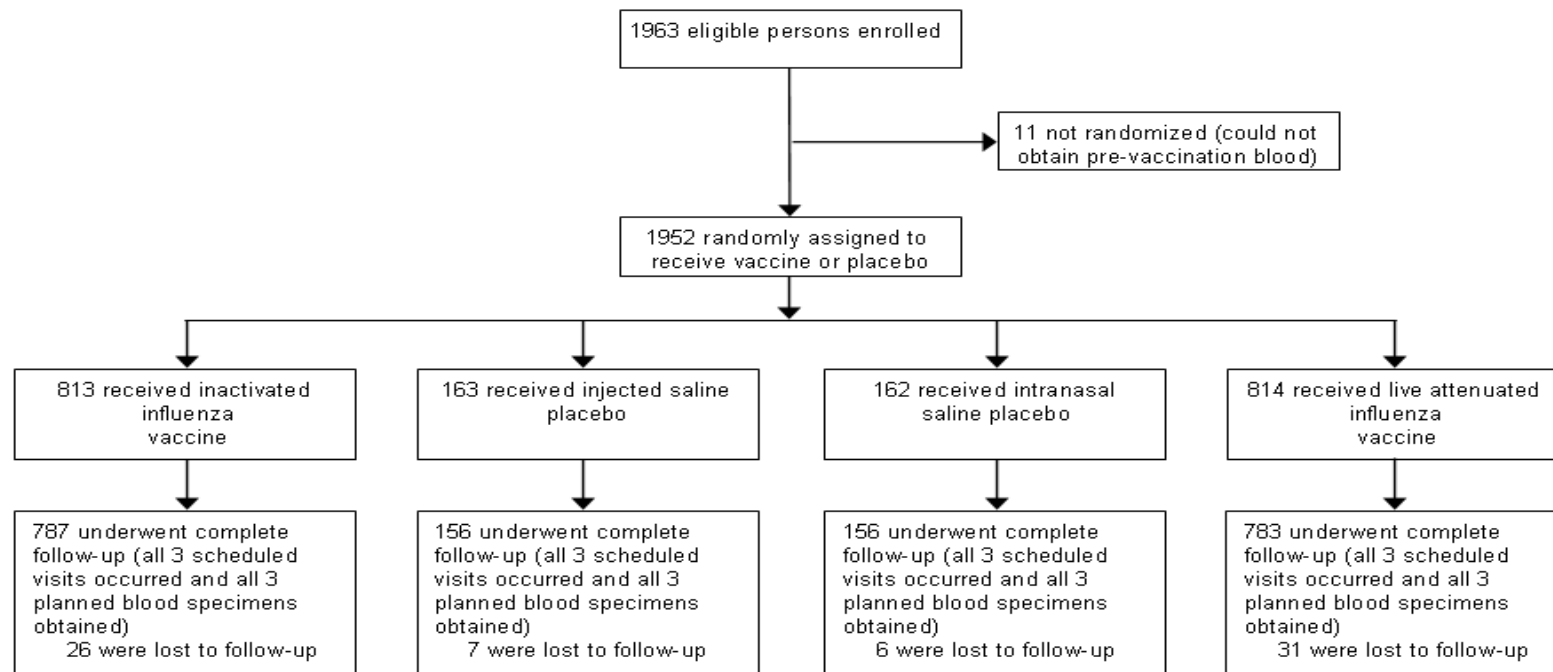


Figure 2. Results of Surveillance during the 2007-2008 Influenza Season in Michigan.

