Article DOI: http://dx.doi.org/10.3201/eid2102.131879

Simulation Study of the Effect of Influenza and Influenza Vaccination on Risk of Acquiring Guillain-Barré Syndrome

Technical Appendix

Details of Simulation Modeling Approach

To simulate observations probabilistically, based on a published relative risk point estimates and 95% CIs, a lognormal distribution was assumed. The mean and standard error on the log scale were then back-calculated from the point estimate and 95% CI and then random draws were taken from the normal distribution with the corresponding mean and standard deviation. These random draws were then exponentiated to yield observations on the original relative risk scale (*1*,*2*). For rates, we took advantage of the fact that the β distribution is a conjugate to binomial data, such that we can draw simulated observations based on a rate and its standard error from a β distribution with appropriately derived shape parameters (*1*,*2*). All simulation parameters and associated statistical uncertainty (i.e., standard errors) were chosen to reflect current peer-reviewed evidence.

Technical Appendix Table 1. Previous studies estimating the relative risk of Guillain-Barré syndrome from influenza vaccination and illness*

Risk, author (reference)	Influenza seasons	Study design	Risk period	Estimated relative risk or odds ratio (95% CI)†
Influenza vaccination				
Lasky et al. (*3*)	1992–1994	Cohort	42 d	1.7 (1.0–2.8)
Juurlink et al. (*4*)	1992–2004	SCCS	2–7 w	1.45 (1.05–1.99)
Hughes et al. (*5*)	1992–2000	SCCS	42 d	0.99 (0.32–3.12)
Tam et al. (*6*)	1991–2001	Case–control	60 d	0.16 (0.02–1.25)
Stowe et al. (*7*)	1990–2005	SCCS	90 d	0.76 (0.41–1.40)
Greene et al. (*8*)	2009–2010	SCRI	42 d	1.3 (0.5–3.8)
Wise et al. (*9*)	2009–2010	Cohort	42 d	1.43 (0.94–1.89)
Kwong et al. (*10*)	1998–2009	SCCS	42 d	1.52 (1.17–1.99)
Galeotti et al. (*11*)	2010–2011	SCCS	42 d	2.1 (1.1–3.9)
Baxter et al. (*12*)	1994–2006	Case-centered	42 d	1.11 (0.39–3.08)
Baxter et al. (*12*)	1994–2006	SCRI	42 d	1.3 (0.75–2.26)
Influenza-like illness				
Tam et al. (*6*)	1991–2001	Case-control	60 d	18.64 (7.49–46.37)
Stowe et al. (*7*)	1990–2005	SCCS	30 d	17.79 (9.77–32.41)
Kwong et al. (*10*)	1993–2009	SCCS	42 d	15.81(10.28–to 24.32)
Galeotti et al. (*11*)	2010–2011	SCCS	42 d	8.7 (4.2–18.3)

*SCCS, self-controlled case series; SCRI, self-controlled risk interval.
†Under the rare disease assumption, Guillain-Barré Syndrome is sufficiently rare that the odds ratio should be a close approximation of the relative risk.

Technical Appendix Table 2. Influenza illness rates from observational studies and control/placebo groups from randomized controlled trials*

Author (reference), study population by age, y	Rate†	Time period (location)	Outcome	Comment
VanTam et al. (*13*)		1966–1984	LCI	Family studies
Children <5	15.3–44.5 (range)			
Children 5–19	16.8–47.7 (range)			
Adults 20–39	16.1–23 (range)			
Adults ≥40	12–21 (range)			
Jefferson et al. (*14*)		1979–2007	LCI	Pooled estimate from all available RCT control arm data
Children <2	9.6 (40/418)			
Children ≤5	19.4 (881/4539)			
Children 6–18	24.9 (175/703)			
Neuzil et al. (*15*)		1974–1999	LCI	RCT control arm data
Children <5	9.5 (95% CI 8.5–10.5)			
Williams et al. (*16*)		2006/2007	LCI	
Health care workers	11.2			
Non–health care workers	10.3			
Kuster et al. (*17*)		1957–2009	LCI	
Health care workers	7.54 (95% CI 4.86–11.70)			
Working adults	5.12 (95% CI 3.08–8.52)			
Jefferson et al. (*18*)		1970–2009	LCI	Pooled estimate from all available RCT control arm data
Healthy adults	2.73 (529/19383)			
Nicholson et al. (*19*) (cited in Jefferson 2010 Cochrane review; analysis 2.2) (*18*)		1992–1994 (UK)	LCI	
Adults ≥60	9.1 (19/209)			
Voordouw et al. (*20*)		1996–1997 (NL)	ICPC codes for influenza	
Adults ≥65	0.35 (32/8911)			
Govaert et al. (*21*)		1991–1992 (NL)	LCI	
Adults ≥60	8.8 (80/911)			
De Villiers et al. (*22*)		2001 (S. Africa)	LCI	
Adults ≥60	7.5 (118/1569)			

*ICPC, International Classification of Primary Care; LCI, laboratory-confirmed influenza; RCT, randomized controlled trial; NL, the Netherlands; S. Africa, South Africa; UK, United Kingdom.
†Rates are expressed as percentages, and when provided by the authors, the 95% CIs or no/total are given in parentheses following the point estimate.

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