"Intra-Seasonal Waning" as Methodological Artifact

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- 3. What if the vaccine is not leaky?

• "Leaky" model: Those susceptible before vaccination have a risk of $\lambda_1 = \lambda_0 \theta$ of becoming infected during a contact if an unvaccinated susceptible has risk λ_0 .

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- Hybrid models:
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Approach

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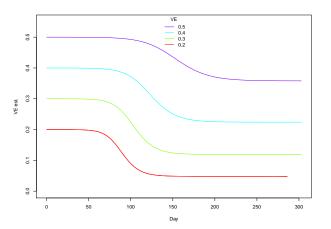
- Simulation of seasonal influenza epidemics using simple SIR ODE models
 - Implement two scenarios ("leaky", "all-or-none" with two viruses)
 - Use numerical solutions to ODEs to generate TND data
 - Calculate VE "estimates" and true VE

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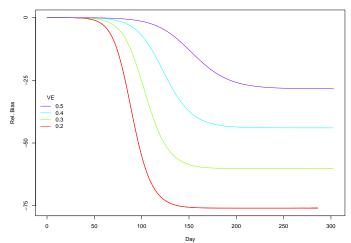
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 - Calculate VE "estimates" and true VE
- Simulation of seasonal influenza epidemics using a stochastic SIR model, keeping track of time since vaccination
 - Implement "all-or-none" with two viruses: A certain proportion of the population, if vaccinated, remains susceptible to virus 1, 2, 1 and 2 or neither
 - Use Ray's analytic approach (only vaccinees, conditional logistic regression)

First scenario: "Leaky" vaccine

Vaccination coverage: 0.47, constant; $R_0 = 1.6$; $\delta = 0.25$

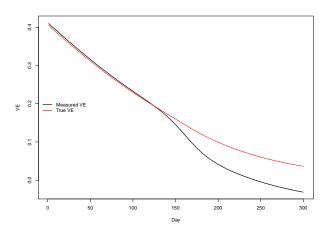


Rel. Bias

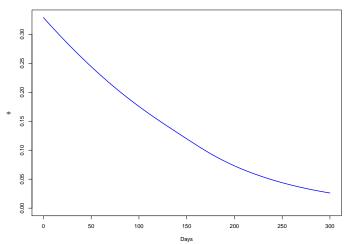


Second scenario: 2 viruses, "all-or-none"

Vaccination coverage: 0.3; $R_0 = 1.25, 1.75; \delta = 0.33$



Time-dependent θ



"All-or-none", 2 viruses, stochastic simulation, time-since-vaccination

- Stochastic simulation with time-since vaccination (TSV)
- Normally-dist. vaccination uptake (cumm. 0.47), starting 100 days before transmission, continuing until 200 days after seeding; R₀ = 1.8, 1.7; Proportion of population susceptible (after vacc.) to virus 1, 2, neither or both: 0.2, 0.4, 0.3, 0.1
- All infections used as cases, control-case ratio 1:3
- Conditional logistic regression, with time since vaccination: < 60, 61 – 120,121 – 180,> 181 days; conditioning on day of enrollment

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Variable	OR
TSV 1	Ref.
TSV 2	3.62
TSV 3	2.13
TSV 4	5.92