

Chapter 6 Rhinovirus

6.1 General overview

Rhinoviruses belong to the Picornaviridae family, small icosahedral viruses made of a protein capsid that encases a single-stranded, positive-sense RNA molecule. About 100 different serotypes have been identified and characterized by their own specific antigens.

Rhinoviruses are responsible for 30 to 50% of adult colds and 10 to 25% of colds in children. Other cold-causing viruses are adenoviruses, coronaviruses, coxsackieviruses, echoviruses, orthomyxoviruses, paramyxoviruses, respiratory syncytial virus, and enteroviruses, each of which produces infections with slightly different patterns of symptoms and severity. Several of the above-mentioned viruses also account for other more severe illnesses (Bella and Rossmann 1999).

6.2 Summary Data

Hendley et al. (1972) inoculated young adult volunteers over the age of 21 with Rhinovirus type 39 (RV 39), strain SF 299, and rhinovirus type 14 (RV 14), strain SF 765, via intranasal exposure route. Shedding of the challenge virus and/or a fourfold or greater increase in titer of serum antibody to a homotypic rhinovirus were accepted as evidence of infection.

Table 6.1. Summary of the rhinovirus data and best fits

Experiment Number	Reference	Host Type/Pathogen Strain	Route/# of Doses	Dose Units	Response	Best Fit Model	Optimized Parameter (s)	LD ₅₀
1	Hendley et al., 1972	humans/ rhinovirus type 14, strain SF 765	oral/6	pfu	infection	Beta-Poisson	$\alpha = 0.20$ $N_{50} = 9.22$	9.22
2	Hendley et al., 1972	humans/ rhinovirus type 39, strain SF 299	oral/6	pfu	infection	-	$\alpha = 0.22$ $N_{50} = 1.81$	1.81

No acceptable fit for experiment 2.

6.3 Optimized Models and Fitting Analyses

6.3.1 Optimization Output for experiment 1

Table 6.2. Human/type 14 strain SF 765 model data

Dose	Infected	Non-infected	Total
3.00E+02	10	2	12
1.50E+02	27	13	40
1.50E+01	6	4	10
5.00E+00	4	6	10
1.50E+00	4	6	10
5.00E-01	1	8	9

Hendley et al., 1972.

Table 6.3. Goodness of Fit and Model Selection

Model	Deviance	Δ	DF	$\chi^2_{0.95,1}$ p-value	$\chi^2_{0.95,m-k}$ p-value
Exponential	51.84	50.16	5	3.84	11.07
Beta Poisson	1.68		4	0	9.49

Beta Poisson is best fitting model

Table 6.4 Optimized parameters for the best fitting (beta Poisson), obtained from 10,000 bootstrap iterations

Parameter	MLE Estimate	Percentiles					
		0.5%	2.5%	5%	95%	97.5%	99.5%
α	0.20	--	--	--	--	--	--
N_{50}	9.22	--	--	--	--	--	--
LD_{50} (spores)	9.22	1.42	2.62	3.35	25.38	31.90	50.18

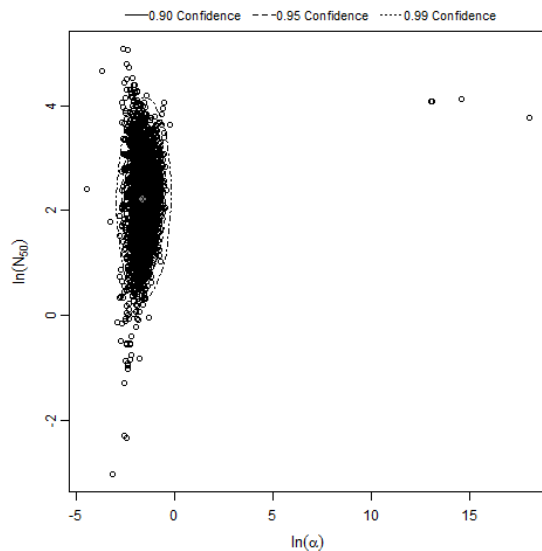


Figure 6.1 Parameter scatter plot for beta Poisson model ellipses signify the 0.9, 0.95 and 0.99 confidence of the parameters.

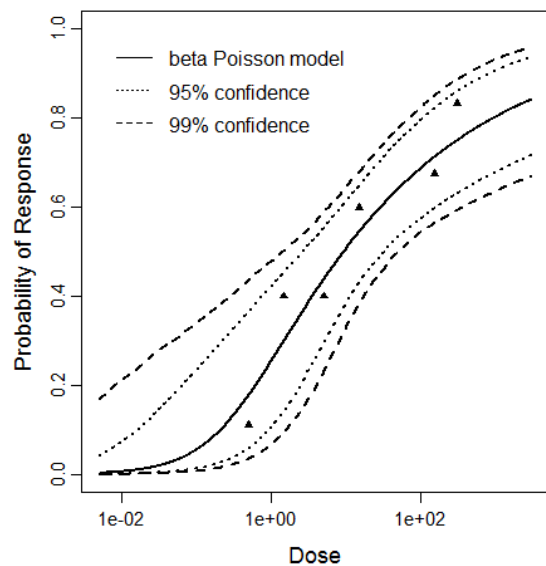


Figure 6.2 beta Poisson model plot, with confidence bounds around optimized model

6.3 Optimized Models and Fitting Analyses

6.3.2 Optimization Output for experiment 2

Table 6.5 Human/type 39 strain SF 299 model data

Dose	Infected	Non-infected	Total
5.00E+01	47	15	62
5.00E+00	5	11	16
1.50E+00	22	11	33
5.00E-01	8	16	24
1.50E-01	2	7	9
5.00E-02	0	11	11

Hendley et al., 1972.

Table 6.6. Goodness of Fit and Model Selection

Model	Deviance	Δ	DF	$\chi^2_{0.95,1}$ p-value	$\chi^2_{0.95,m-k}$ p-value
Exponential	129.77	117.41	5	3.84	11.07
Beta Poisson	12.36		4	0	9.49

Beta Poisson is best fitting model

Table 6.7 Optimized parameters for the best fitting (beta Poisson), obtained from 10,000 bootstrap iterations

Parameter	MLE Estimate	Percentiles					
		0.5%	2.5%	5%	95%	97.5%	99.5%
α	0.22	--	--	--	--	--	--
N_{50}	1.81	--	--	--	--	--	--
LD_{50} (spores)	1.81	0.69	0.87	0.98	3.76	4.52	inf

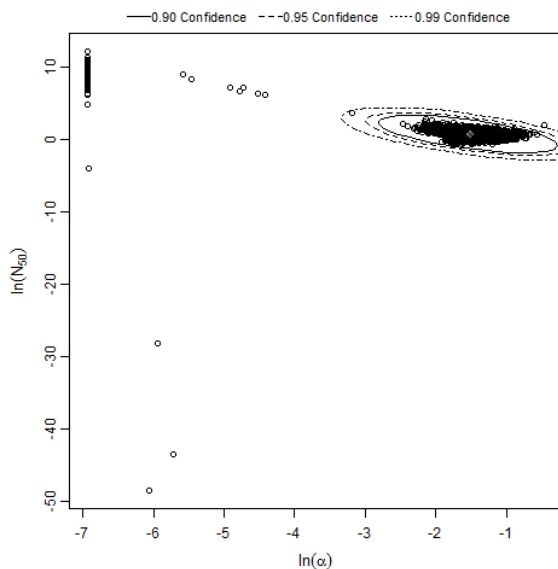


Figure 6.3 Parameter scatter plot for beta Poisson model ellipses signify the 0.9, 0.95 and 0.99 confidence of the parameters.

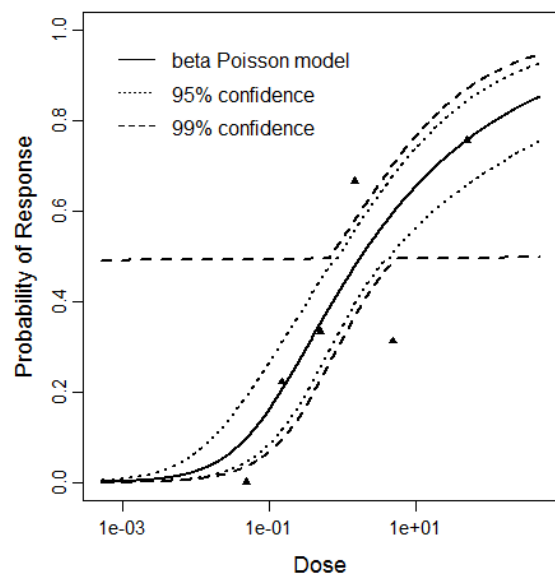


Figure 6.4 beta Poisson model plot, with confidence bounds around optimized model

6.4. Summary

The responses caused by doses less than one observed in these two experiments should be due to the uncertainties of dose counting in the original study.

References

Bella, J. and Rossmann, M.G. (1999) Review: Rhinoviruses and their icam receptors. *Journal of Structural Biology* **128**, 69–74.

Hendley, J.O., Edmondson Jr., W.P. and Gwaltney Jr., J.M. (1972) Relation between naturally acquired immunity and infectivity of two rhinoviruses involunteers. *Journal of Infectious Diseases* **125**, 243-248.