CHAPTER THREE

TOXICITY TESTING

3.1 Introduction

In order to protect freshwater resources from possible pollutants in fertilizers, pesticides, and industrial and municipal discharges, the government regularly monitors the toxicity level of effluents based on different tests to ensure the safety of the environment. One testing approach is the *Ceriodaphnia dubia* survival and reproduction toxicity test. This test is an accepted standard method in the assessment of the toxicity of effluents, environmental samples, and single chemicals (Weber et al., 1989).

Traditionally, interest in toxicity studies is focused on mortality, the acute effect. Recent focus had shifted to chronic effects such as growth or fecundity and the *Ceriodaphnia* test is perhaps the most common of the chronic tests. The experimental design consists of placing organisms in beakers or growth chambers, treating the units with the chemical or dose of interest and monitoring the number of organisms over time (usually seven days). The traditional method in analyzing these data is to apply statistical tests based on analysis of variance followed by pairwise tests to detect treatment concentrations that differ from the control group. Contemporary methods use regression models based on a generalized linear model framework (Kerr and Meador, 1996) or a quasi-likelihood technique (Kaur et al., 1995).

When mortalities occur, the response of interest is often complicated. The methods mentioned above are limited to separate analysis of mortality and fecundity. Since mortality almost always exists during the test (especially for high doses), this creates extra zeroes in the response and the above methods may be inappropriate and produce biased estimates. Morgan (1992) discussed the use of Abbott's formula (Abbott, 1925) and other methods to adjust the natural or control mortality in mortality modeling. However, not much has been done in chronic toxicity testing. In order to incorporate these extra zeroes due to mortality, a mixture approach is proposed in this chapter to model and analyze the fecundity data with adjustment for mortality effects. This model allows zeroes to be produced from two different sources, mortality and nonreproductive organisms. The response Y (number of offspring) depends on two variables X and Z via the model Y = X*Z, where X is a nonnegative variable representing the number of offspring and Z is a dichotomous variable representing mortality with Z = 0 or 1. When mortality information is provided, both Z and Y are observed. However, most of the time, mortality information is missing and only Y is observable. This mixture model accounts for a certain number of animals who die before any eggs are produced. However, the model does not account for the actual time of death. Time of death can be incorporated into the model and will be discussed in a later chapter. Another major interest of chronic toxicity testing is potency estimation, which indicates the effect of the toxicant on reproduction or growth. The current potency estimate and a new combined potency estimate which incorporates both mortality and fecundity effects are also described.

3.2 Current Potency Estimators

Currently, there are two commonly used methods for analyzing and estimating inhibition concentration from these toxicity tests. They are the chronic value (ChV) procedure and the inhibition concentration (IC) procedure. The ChV procedure is based on analysis of variance and uses sequential statistical tests to detect treatment concentrations that differ from the control group. Either parametric or nonparametric hypothesis tests are recommended depending on the distributional assumptions considered for the response variable (Weber et al., 1989). The no-observed effect concentration (NOEC) and the lowest-observed effect concentration (LOEC) are obtained based on estimates of the inhibition concentration and the chronic value. The NOEC is the highest concentration level where the mean response does not differ statistically from the mean response of the control group (zero concentration group). And the LOEC is the lowest concentration level where the mean response is observed to be statistically different from the mean response in the control group. A point estimate of the safe concentration, the chronic value (ChV), is then calculated as the geometric mean between these two concentration. Since the ChV calculation is based on a hypotheses testing procedure, it is highly dependent on the sample sizes (Oris and Bailer, 1993; Suter, 1996). The chronic value estimate also depends on the design of the experiment because the LOEC and the NOEC can only be values that are tested concentration levels.

On the other hand, the IC procedure is a regression based approach which involves the point estimation of an inhibition concentration (IC_{100*q}) endpoint that causes a specified percent reduction (100*q%) in reproduction output (Weber et al., 1989; Oris et al., 1991; Norberg-King, 1988). In general, IC_{100*q} is the concentration of the toxicant required to induce a 100*q% level of reproduction inhibition where $0<q<1$. The concentration of interest is the concentration where the mean response is a proportion (1-q) of the mean response of the control group, which can be represented symbolically as the concentration x such that:

$$1-q = (\mu_x / \mu_C)$$

and μ_C is the mean response of the control. This analysis usually assumes that reproduction decreases monotonically as the concentration of the toxicant increases. There are a variety of approaches for the estimation of IC’s including inverse regression and interpolation. For the interpolation method, linear interpolation between the two nearest concentration values which produce inhibition levels above and below the specified percentage is used to calculate the point estimate of the endpoint. Hence, in order to obtain the IC_{50}, the value $\mu_x = 0.5*\mu_C$ is needed. It has been observed that the 50% inhibition point (IC_{50}) roughly corresponds to calculated ChV (= geometric mean of

LOEC and NOEC) values and that the 25% inhibition point (IC_{25}) corresponds roughly to NOECs from hypothesis-testing analyses (Oris et al., 1991; Norberg-King, 1988). The EPA currently recommends the IC_{25} as the preferred endpoint for compliance monitoring (USEPA, 1990).

The linear interpolation used in the IC procedure often obtains unsatisfactory results because the linear assumption may not be appropriate. Also since the calculation uses the observed means, the estimate can be affected by outliers or atypical values. Quite often these are zero observations due to mortality.

Many authors have suggested regression type models based on a dose-response relationship to improve the IC procedure and discuss the advantages of using them in chronic toxicity testing (Stephen and Rogers, 1985). Bailer and Oris (1993) proposed a concentration-response model as an alternative to the ChV calculation and the linear interpolation method. They modeled the relationship between exposure concentration and total number of offspring and estimated concentrations that led to some specified level of inhibition relative to the control group. Bailer and Oris (1993) found that the commonly used Poisson assumption is adequate for their model involving count data. Other authors also proposed regression type models based on the generalized linear model framework (Kerr and Meador, 1996) and the quasi-likelihood technique (Kaur et al., 1995).

3.3 Mixture model

Even though the proposed regression type models have many advantages over the ChV and IC methods in chronic toxicity testing, they can only analyze fecundity apart from the mortality effect or model only mortality. Since mortality typically occurs for some organisms during the test, mortality often complicates the response of interest. Approaches based on ignoring animals which die, or treating fecundity as zero are inappropriate and produce biased estimates. In order to incorporate these extra zeroes due to mortality, a mixture approach is proposed to model and to account for mortality and analyze the fecundity data. The mixture approach has been applied in other fields. As discussed in the previous chapter, Lachenbruch (1976), Feuerverger (1979), Heilbron (1989), and Lambert (1992) all developed different techniques using mixture approach to model different type of data.

In this chapter, I look at a *Ceriodaphnia dubia* reproduction toxicity test where the observations are the egg counts of the organisms. The model allows zeroes to be produced from two different sources, mortality and nonreproductive organisms. The response Y (number of offspring) depends on two variables X and Z via the model Y = X*Z, where X is a nonnegative variable representing the number of offspring and Z is a dichotomous variable representing mortality with Z = 0 or 1. When mortality information is provided, both Z and Y are observed. However, most of the time, mortality information is missing and only Y is observable. This mixture model accounts for a certain number of animals who die before any eggs are produced. The analysis of the mixture model is based on the likelihood function of the model. The most common distribution for count data is the Poisson distribution. Bailer and Oris (1993) used the Poisson model in their analysis involving count data. The Poisson and zero mixed Poisson distributions are represented in Table 3.1 along with their means and variances.

3.4 Chronic Toxicity Testing with adjustment of mortality effects

A typical chronic toxicity test uses less than 12-hour-old juveniles and measures reproductive output of 10-20 individuals for each treatment in a 7-day period. We refer to “treatment” as the effluent which is a mix of toxicants or a single chemical. One organism is placed in each container and a dose treatment is applied. Each treatment is usually replicated ten to twenty times depends on the individual experiment. The number of eggs produced each day is counted and the experiment is run for seven days. The response is the number of eggs produced by each organism during the seven day period. The analysis is done on the total number of eggs over the seven day period for

Table 3.1. The means and variances for the zero mixed Poisson and Poisson distributions. λ is the mean number of offspring and p is the probability of death.

Distribution	Poisson	Zero mixed Poisson*
Density	$P(X = x) = \frac{e^{-\lambda}\lambda^{x}}{x!}$ $x = 0, 1, 2, \ldots$	$P(X = 0) = p + (1 - p)e^{-\lambda}$ $P(X = x) = (1 - p)\frac{e^{-\lambda}\lambda^{x}}{x!}$ $x = 1, 2, 3, \ldots$ and $0 < p < 1$
Mean	λ	$(1 - p)\lambda$
Variance	λ	$(1 - p)\lambda + p(1 - p)\lambda^2$

* Heilbron (1989)

each treatment. If the dose is sufficiently great, there is mortality and a high zero count may occur. A mixture model is used to adjust the mortality effects. Since the responses (Y's) are egg counts, the model would assume that the counts are independent, that mortality occurs with certain probability p_i (for the ith dose of the treatment) and the counts follow a Poisson distribution with mean λ. Hence, this mixture model accounts for a certain number of animals who die before any eggs are produced. This model is an added zero model which involves mixed zeroes from mortality and non-reproduction.

The Model

The n responses $\underline{Y} = (Y_1, \ldots, Y_n)'$ are independent with

$$\textit{Prob}\ (Y_i = 0) = p_i + (1 - p_i)e^{-\lambda_i}$$

$$\textit{Prob}\ (Y_i = k) = (1 - p_i)e^{-\lambda_i}\lambda_i^{k}/k!, \text{ where } k > 0.$$

The relationship with dose may be modeled generally through the parameters $\underline{\lambda} = (\lambda_1, ..., \lambda_n)'$ and $\underline{p} = (p_1, \ldots, p_n)'$ using the linear model

$$\log(\underline{\lambda}) = \mathbf{B}\underline{\beta} \text{ and } \operatorname{logit}(\underline{p}) = \log(\underline{p}/(1 - \underline{p})) = \mathbf{G}\underline{\gamma}$$

for the covariate matrices (doses) **B** and **G** and parameters $\underline{\beta}$ and $\underline{\gamma}$.

Approaches to modeling this mixture depend on whether $\underline{p}$ and $\underline{\lambda}$ are unrelated or related. In the present example, we assume that $\underline{p}$ and $\underline{\lambda}$ are unrelated and also that the covariates that affect the Poisson mean are the same as the covariates that affect the probability p, i.e., $\mathbf{B} = \mathbf{G}$. Under this assumption the mixture model requires twice as many parameters as the Poisson regression model. By assuming an extra random variable Z_i to indicate the source of zero observations, where $Z_i = 0$ if the observation Y_i is from the Poisson part and $Z_i = 1$ otherwise, the likelihood function of the model can easily be broken down into several parts. An E-M algorithm can then be used to obtain the maximum likelihood estimators for the coefficients of the ZIP model treating the Z_i's as incomplete information. By pre-assigning initial values to the parameters, the EM algorithm would iteratively calculate the estimates until convergence. The EM algorithm for ZIP regression based on Lambert (1992) was implemented using the S-plus programming language. The program is presented in Appendix. The details of the E-M algorithm are presented in the following section.

3.5 E-M algorithm

Since the analysis is based on the likelihood function, we start with writing down the log likelihood of the zero inflated Poisson model. By replacing the parameters $\underline{l}$ and $\underline{p}$ with $e^{\mathbf{B}b}$ and $1/(1+ e^{-\mathbf{G}g})$, the log likelihood function of the data can be written as the following:

$$L(\gamma, \beta; y) = \sum_{y_i=0} \log(e^{G_i\gamma} + \exp(-e^{B_i\beta})) + \sum_{y_i>0}(y_i B_i\beta - e^{B_i\beta}) - \sum_{i=1}^{n} \log(1+e^{G_i\gamma}) - \sum_{y_i>0}\log(y_i!) \qquad (3.1).$$

where $\mathbf{G}_i$ and $\mathbf{B}_i$ are the i th row of the covariate matrix **G** and **B,** β and γ are vectors of the regression coefficients. This function is rather difficult to maximize because of the sum of the two exponentials in the first term. Now we assume that we know where the zeroes came from, and we further define an extra variable Z_i, where $Z_i = 0$ if the observation Y_i is from a surviving animal (Poisson) and $Z_i = 1$ if the observation Y_i is from mortality (subpopulation of zeroes). Then, imagine that we are able to observe both y and z, the likelihood function L(γ, β; y) can be written as the following:

$$L(\gamma, \beta; y, z) = \sum_{i=1}^{n}(z_i\mathbf{G}_i\gamma - \log(1+e^{\mathbf{G}_i\gamma})) + \sum_{i=1}^{n}(1-z_i)(y_i\mathbf{B}_i\beta - e^{\mathbf{B}_i\beta}) - \sum_{i=1}^{n}(1-z_i)\log(y_i!) \qquad (3.2).$$

This consists of 3 components:

$$1.\ L(\gamma; y, z) = \sum_{i=1}^{n}(z_i\mathbf{G}_i\gamma - \log(1+e^{\mathbf{G}_i\gamma})) \qquad (3.3)$$

$$2.\ L(\beta; y, z) = \sum_{i=1}^{n}(1-z_i)(y_i\mathbf{B}_i\beta - e^{\mathbf{B}_i\beta}) \qquad (3.4)$$

$$3.\ \sum_{i=1}^{n}(1-z_i)\log(y_i!) \qquad (3.5)$$

Part 3 can be ignored in the maximization process because it is just a constant term with respect to the regression coefficients β and γ. The log likelihood can then be maximized rather easily because 1 and 2 can be maximized separately. However, the variable Z is unobservable and the E-M algorithm is introduced to solve this problem. The E-M algorithm involves two steps: the E (estimation) step and the M (maximization) step. The likelihood can then be maximized iteratively by alternating between the two steps. The E step is to estimate the value of Z given the current estimates of β and γ. The M step is to estimate the value of β and γ by maximizing the likelihood given the current value of Z. The actual algorithm consists of three steps for each iteration, one estimation step, one maximization step for β and one maximization step for γ, for the $k+1^{th}$ iteration. The details are:

1. E-step

Estimate Z_i by using Bayes rule given the most recent estimates of β and γ, $\beta^{(k)}$ and $\gamma^{(k)}$. Here $Z_i^{(k)} = Prob(\text{mortality}|y_i, g^{(k)}, b^{(k)})$

$$= \frac{Prob(y_i \mid \text{mortality})Prob(\text{mortality})}{Prob(y_i \mid \text{mortality})Prob(\text{mortality}) + Prob(y_i \mid \text{survival})Prob(\text{survival})}$$

$$= (1+e^{-G_i g^{(k)} - \exp(B_i b^{(k)})})^{-1} \qquad \text{if } y_i = 0$$

$$= 0 \qquad \text{if } y_i > 0 \qquad (3.7)$$

2. M step for β

Maximize $L(b; y, Z^{(k)})$ to obtain the estimate of $\beta^{(k+1)}$. This can be found by a weighted log-linear Poisson regression with weights $1- Z^{(k)}$ [McCullagh and Nelder (1989)].

3. M step for γ

Maximize $L_c(g; y, Z^{(k)})$ to obtain the estimate of $g^{(k+1)}$. Since $Z_i^{(k)} = 0$ whenever $y_i > 0$,

$L(g; y, z) = \sum_{i=1}^{n} (z_i G_i g - \log(1+e^{G_i g}))$ can be re-written as

$$L(g; y, z) = \sum_{y_i=0} Z_i^{(k)} G_i g - \sum_{y_i=0} Z_i^{(k)} \log(1+e^{G_i g}) - \sum_{i=1}^{n} (1-Z_i^{(k)}) \log(1+e^{G_i g}) \qquad (3.8).$$

To maximize this as a function of g, suppose that n_0 out of n y_i's are zeroes, for example, $y_{i_1},\ldots,y_{i_{n_0}}$ are 0. We can define the following:

$$\boldsymbol{y}_*' = (y_1, \ldots, y_n, y_{i_1}, \ldots, y_{i_{n_0}}),$$

$$\mathbf{G}_*' = (\mathbf{G}_1', \ldots, \mathbf{G}_{i_1}', \ldots, \mathbf{G}_{in_0}'),$$

$$\mathbf{P}_*' = (p_{1, \ldots,} p_n, p_{i_1}, \ldots, p_{i_{n_0}}).$$

Then we also define a diagonal matrix $\mathbf{W}^{(k)}$ with diagonal element

$$w^{(k)} = (1 - Z_1^{(k)}, \ldots, 1 - Z_n^{(k)}, Z_{i_1}^{(k)}, \ldots Z_{i_{n_0}}^{(k)}).$$

Now we can write,

$$\mathrm{L}(\gamma;\, \mathrm{y},\, \mathrm{Z}^{(k)}) = \sum_{i=1}^{n+n_0} \mathrm{y}_{*i} \mathrm{w}_i^{(k)} \mathrm{G}_{*i}\gamma - \sum_{i=1}^{n+n_0} \mathrm{w}_i^{(k)} \log(1 + e^{\mathrm{G}_{*i}\gamma}) \qquad (3.9)$$

with the score function $\mathbf{G}_*'\mathbf{W}^{(k)}(\mathbf{y}_* - \mathbf{P}_*)$ and the negative information matrix $\mathbf{G}_*'\mathbf{W}^{(\mathbf{k})}\mathbf{Q}_*\mathbf{G}_*$,where $\mathbf{Q}_*$ is the diagonal matrix with $\mathbf{P}_*(1-\mathbf{P}_*)$ on the diagonal. These functions are the same as those for a weighted logistic regression with response y_*, covariate matrix $\mathbf{G}_*$, and weights $w^{(k)}$. Hence $\gamma^{(k)}$ can be found easily by weighted logistic regression.

The E-M algorithm starts with an initial values of β and γ and iterates through the E step and M step until the estimates converge. The initial values of β can be found by performing a Poisson regression on only the positive responses. If mortality information is recorded during the experiment, the initial values of γ can be found by a logistic regression using the mortality information. However, if the mortality information was not recorded, the initial values of γ can be found by estimating the intercept term by the log odds of the observed average probability and setting other terms to zeroes. The initial value of z will then be determined by the values of β and γ.

In the case where $\underline{p}$ and $\underline{\lambda}$ are related, one approach is to re-parametrize the model as $\log(\underline{\lambda}) = \mathbf{B}\beta$ and $\operatorname{logit}(\underline{p}) = -\tau\mathbf{B}\beta$, with an unknown, real-valued shape parameter τ which implies that $p_i = (1+ \lambda_i^{\tau})^{-1}$. The ZIP model with logit link for $\underline{p}$, log link for $\underline{\lambda}$, and shape parameter τ is denoted as ZIP(τ). A Newton Raphson algorithm can be used to estimate the coefficients for the ZIP(τ) regression model which is computationally more complex than the E-M algorithm and not discussed in this dissertation.

3.6 Examples

The model was applied to an experiment involving four chemicals (copper, mercury, zinc and chromium). The experiment is carried out by placing a water flea (*Ceriodaphnia dubia*) into a container and different levels of toxicants. There are 33 treatments in the experiment with 20 replications for each treatment. The total egg counts for the seven days period are used as the response. Thus the same data is used throughout only with different independent variables in the different models. In order to keep the comparison of the inhibition concentration simple, only the single covariate models are compared in the first example. Models that include all toxicants will be presented later. Here, the Poisson regression approach was first carried out. Table 3.2 presents the results of fitting Poisson models to each chemical.

Table 3.2. Summary of Poisson models each with single toxicant. Values in () are standard errors.

	CH	CU	ME	ZI
β_0	2.811 (0.0151)	2.876 (0.0143)	2.838 (0.0123)	2.662 (0.0171)
β_1	-0.208 (0.0097)	-0.096 (0.0036)	-0.120 (0.0035)	-0.005 (0.0006)
SSR	1619.827	1239.807	1081.763	1858.07
log likelihood	-4037.65	-3654.33	-3585.16	-4253.16

Note: log likelihood is calculated based on all data, SSR is calculated based on treatment means.

This approach assumes that mean fecundity follows a Poisson distribution, but it does not consider the mortality effect on the responses. The copper model and the mercury model are the best Poisson models among the four models with the highest log-likelihood (-3654.33 for copper and –3585.16 for mercury). The mixture model approach was based on ZIP model (Lambert, 1992) and the results are presented in Table 3.3. The model is fitted using an Splus program (Appendix B).

Table 3.3. Summary of ZIP regression models each with single toxicant. β_0, β_1, are the Poisson regression and γ_0, γ_1 are for the binary model. Values in () are standard errors.

	CH	CU	ME	ZI
β_0	2.900 (0.0155)	2.944 (0.0142)	2.960 (0.0124)	2.895 (0.0166)
β_1	-0.052 (0.0102)	-0.037 (0.0036)	-0.060 (0.0035)	-0.002 (0.00060)
γ_0	-2.064 (0.1658)	-1.800 (0.1231)	-1.985 (0.1496)	-1.310 (0.1529)
γ_1	0.605 (0.0773)	0.131 (0.0151)	0.222 (0.0243)	0.009 (0.0051)
SSR	1604.479	1304.269	1098.168	1860.810
log likelihood	-2178.63	-2107.96	-2023.39	-2218.50

Note: log likelihood is calculated based on all data, SSR is calculated based on treatment means.

The copper model and the mercury model are the best among the four models with the highest log-likelihood (–2107.96 for copper and –2023.39 for mercury, Table 3.3). However, the mixture model has 4 parameters which is 2 more than the Poisson model. Different hypotheses can be tested based on the likelihood ratio test. One of them is the hypothesis that the Poisson model is better than the ZIP model. The test statistic follows an asymptotic chi-square distribution and for the copper (CU) model 2x(3654.33–2107.96) = 2x1546.34 = 3092.68 with (4 – 2) = 2 degrees of freedom. This is highly significant and indicates that the ZIP model is better than the regular Poisson model. In fact, based on the log likelihood, all four model are improved by including the zero inflated model. The fitted models for copper and mercury are plotted in Figure 3.1 and 3.2 respectively.

Figure 3.1. Copper Model (PDF, 4K, Fig3-1.pdf)

Figure 3.2. Mercury Model (PDF, 4K, Fig3-2.pdf)

Both the Poisson model and mixture model are plotted. The mixture model involves two different parts, the overall prediction is based on the product of two parts [$\hat{\mu} = (1 - \hat{p})*\hat{\lambda}$] where $\hat{\lambda}$ is the Poisson mean (reproduction) and $(1 - \hat{p})$ is the logistic (survival) probability. The survival probabilities are plotted at the bottom of the graphs and they show mercury has a greater mortality effect than copper (the survival probability of mercury drops off faster than that of copper). The plots also show that the mixture model is very comparable to the Poisson model. However, the overall fits are affected by the large variation in the observations and the poor design of the experiment. Further research should investigate the design of experiments for mixture models. This may improve the fit of the model as well as help to reduce the variation in the data.

A second example of the *Ceriodaphnia* data includes all four toxicants in the models at the same time. Furthermore, the interactions and quadratic terms are also considered. Six different models are investigated, and the estimated coefficients of these six models are presented in Table 3.4 – Table 3.8. The regular Poisson model results are also shown next to the ZIP model results for comparisons. The comparisons are done based on the log likelihood and are shown in Table 3.9. The terms used in the models are explained in Table 3.10.

Based on the log likelihood values in Table 3.9, model #5 with 10 parameters has the highest value (-2859.15) among all the ZIP models. This model has the same number of parameters as model #6, but its value of log likelihood is (2946.52 – 2859.15 = 87.37) higher than model #6. The toxicant, zinc is dropped in models #4 and #5 because it was shown to have a very weak toxicant effect in the previous example.

Model #1 and model #2 have the lowest log likelihood (-3188.10 and –3115.36 respectively) among all the ZIP models. When compared with the Poisson model, model #3, 4, 5, 6 of the ZIP model have a higher log likelihood values than those of the Poisson models. The differences in the log likelihood of the Poisson model and the ZIP for model #3 is 94, for model #4 is 188.5, for model #5 is 286.18, and for model #6 is 244.71. These values are all significant when using the likelihood ratio test. Hence, the Poisson models are the better models in these cases. On the other hand, model #1 and #2 of Poisson model have higher log likelihood values than those of #1 and #2 of ZIP models. The Poisson models fit a little bit better in these two models.

Table 3.4. Estimated coefficients for ZIP and Poisson models

		Model #1	Model #1	Model #2	Model #2
		ZIP	Poisson	ZIP	Poisson
Reproduction (Poisson part for ZIP)	INT	3.028 (0.0218)	3.004 (0.0219)	3.056 (0.0206)	3.080 (0.0203)
	CH	0.105 (0.0525)	0.264 (0.0478)	-0.023 (0.0341)	0.136 (0.0344)
	CU	0.027 (0.0227)	0.031 (0.0209)	0.006 (0.0119)	-0.015 (0.0120)
	ME	-0.277 (0.0377)	-0.330 (0.0297)	-0.187 (0.0227)	-0.286 (0.0210)
	ZI	-0.011 (0.0025)	-0.015 (0.0025)	-0.007 (0.0024)	-0.009 (0.0024)
	CH*CU	0.003 (0.0056)	0.027 (0.0047)	--	--
	CH*ME	-0.0005 (0.0050)	-0.035 (0.0037)	--	--
	CH*ZI	-0.006 (0.0008)	-0.006 (0.0009)	--	--
	CU*ME	-0.006 (0.0017)	-0.010 (0.0013)	--	--
	CU*ZI	-0.00011 (0.0005)	-0.003 (0.0005)	--	--
	ME*ZI	0.001 (0.0003)	0.001 (0.0003)	--	--
	CH*CH	-0.004 (0.013)	-0.089 (0.0107)	-0.005 (0.0105)	-0.093 (0.0011)
	CU*CU	-0.002 (0.0007)	-0.002 (0.0006)	-0.001 (0.0005)	-0.002 (0.0005)
	ME*ME	0.024 (0.0035)	0.032 (0.0028)	0.015 (0.0026)	0.024 (0.0240)
	ZI*ZI	0.0003 (0.0001)	0.0005 (0.000057)	0.0002 (0.00005)	0.0002 (0.0005)

Table 3.5. Estimated coefficients for the mortality part of ZIP models

		Model #1	Model #2	Model #3
		ZIP	ZIP	ZIP
Mortality (logistic part of ZIP)	INT	-4.925 (0.9608)	-5.172 (0.5850)	-3.887 (0.570)
	CH	-1.202 (0.5318)	0.0314 (0.2983)	1.016 (0.2126)
	CU	-0.134 (0.2018)	0.301 (0.1150)	0.014 (0.0558)
	ME	1.623 (0.3328)	0.790 (0.1844)	0.107 (0.0972)
	ZI	0.148 (0.0432)	0.117 (0.0313)	-0.008 (0.0212)
	CH*CU	-0.099 (0.0209)	--	-0.072 (0.0194)
	CH*ME	0.090 (0.0373)	--	0.038 (0.0290)
	CH*ZI	0.013 (0.0082)	--	-0.007 (0.0075)
	CU*ME	0.013 (0.0064)	--	0.007 (0.0060)
	CU*ZI	0.013 (0.0041)	--	0.011 (0.0031)
	ME*ZI	-0.011 (0.0034)	--	-0.001 (0.0021)
	CH*CH	0.483 (0.1160)	0.185 (0.0770)	--
	CU*CU	0.006 (0.0061)	-0.006 (0.0043)	--
	ME*ME	-0.156 (0.0343)	-0.068 (0.0201)	--
	ZI*ZI	-0.003 (0.0007)	-0.002 (0.0006)	--

Table 3.6. Estimated coefficients for ZIP and Poisson models

		Model #3	Model #3	Model #4	Model #4
		ZIP	Poisson	ZIP	Poisson
Reproduction (Poisson part of ZIP)	INT	3.036 (0.0211)	3.033 (0.0210)	3.029 (0.0187)	3.057 (0.0184)
	CH	0.046 (0.0229)	-0.113 (0.0225)	-0.057 (0.0167)	-0.149 (0.0160)
	CU	-0.043 (0.0081)	-0.046 (0.0079)	-0.025 (0.0048)	-0.067 (0.0048)
	ME	-0.033 (0.0100)	-0.007 (0.0100)	-0.016 (0.0077)	0.004 (0.0072)
	ZI	-0.002 (0.0014)	0.006 (0.0010)	--	--
	CH*CU	0.015 (0.0055)	0.039 (0.0035)	0.017 (0.0055)	0.034 (0.0053)
	CH*ME	-0.011 (0.0039)	-0.0372 (0.0008)	-0.011 (0.0037)	-0.039 (0.0033)
	CH*ZI	-0.004 (0.0007)	-0.0027 (0.0016)	--	--
	CU*ME	-0.008 (0.0016)	-0.014 (0.0003)	-0.008 (0.0017)	-0.014 (0.0015)
	CU*ZI	0.001 (0.0039)	-0.002 (0.0004)	--	--
	ME*ZI	-0.001 (0.0002)	0.0001 (0.0002)	--	--

Table 3.7. Estimated coefficients for ZIP and Poisson models

		Model #5	Model #5	Model #6	Model #6
		ZIP	Poisson	ZIP	Poisson
Reproduction (Poisson part of ZIP)	INT	3.031 (0.0178)	3.101 (0.0171)	3.049 (0.0191)	3.113 (0.0186)
	CH	-0.032 (0.0105)	-0.139 (0.0100)	-0.031 (0.0111)	-0.136 (0.0106)
	CU	-0.015 (0.0036)	-0.043 (0.0034)	-0.023 (0.0034)	-0.063 (0.0033)
	ME	-0.038 (0.0050)	-0.059 (0.0051)	-0.055 (0.0036)	-0.090 (0.0037)
	ZI	--	--	-0.00008 (0.0007)	0.002 (0.0007)
	CU*ME	-0.005 (0.0011)	-0.009 (0.0011)	--	--

Table 3.8. Estimated coefficients for the mortality part of ZIP models

		Model #4	Model #5	Model #6
		ZIP	ZIP	ZIP
Mortality (logistic)	INT	-3.598 (0.3688)	-3.528 (0.2788)	-3.943 (0.3566)
	CH	0.823 (0.1506)	0.649 (0.0972)	0.665 (0.1006)
	CU	0.185 (0.0259)	0.145 (0.0224)	0.136 (0.0179)
	ME	0.100 (0.0683)	0.187 (0.0345)	0.171 (0.0283)
	ZI	--	--	0.016 (0.0065)
	CH*CU	-0.068 (0.0203)	--	--
	CH*ME	0.028 (0.0259)	--	--
	CU*ME	0.007 (0.0064)	-0.004 (0.0034)	--

Table 3.9. Comparison of ZIP and Poisson model

Models	p (ZIP)	SSR-ZIP	SSR-Poisson	Log (likelihood) ZIP	Log (likelihood) Poisson
X+ interactions + quadratic (#1)	30	385.44	474.00	-3188.10	-2908.88
X+ interactions (#3)	22	591.00	1104.51	-2942.07	-3036.07
X + quadratic (#2)	18	561.72	430.66	-3115.36	-3101.69
CH, CU, ME, CH*CU, CH*ME, CU*ME (#4)	14	663.58	1070.77	-2876.01	-3064.51
CH, CU, ME, CU*ME (#5)	10	682.59	861.15	-2859.15	-3145.33
X (#6)	10	679.80	379.51	-2946.52	-3191.03

Table 3.10. Explanation of the terms in the models

Covariates	Terms	# of terms
X	Chromium (CH), Copper (CU), Mercury (ME), Zinc (ZI)	4
interactions	CH*CU, CH*ME, CH*ZI, CU*ME, CU*ZI, ME*ZI	6
quadratic	CH^2, CU^2, ME^2, ZI^2	4

3.7 Inhibition Concentrations (ICx) and the Confidence Intervals

The examples in previous section show how the mixture model is compared to the regular Poisson model. Researchers are often interested in obtaining some kind of potency estimator to look at the strength of different toxicants. In this section, a potency estimator, inhibition concentration, is discussed. Since the mixture model involves two different parts, the overall prediction is based on the product of two parts [$\hat{\mu}$ = (1 - $\hat{p}$)*$\hat{\lambda}$]. The Poisson part of the mixture model is $\hat{\lambda} = e^{x\underline{\hat{\beta}}}$ and the logistic part of the model is $\hat{p} = \dfrac{1}{1+e^{-x\underline{\hat{\gamma}}}}$. As mentioned in the previous section, IC $_{100*q}$ is the concentration of the toxicant required to induce a 100*q% level of reproduction inhibition where 0<q<1. For the mixture approach, the inhibition concentration can still be calculated using the regular definition, however, the formula is based on the mixture model. The concentration of interest is where the mean response is a proportion (1-q) of the mean response of the control group, which can be represented symbolically as the concentration x such that

$$1\text{-}q = (\mu_x / \mu_C) \tag{3.10}$$

and μ_C is the mean response of the control. Assuming the simplest single covariate (monotonic decreasing) model, the overall model prediction is $\hat{\mu}_x = \hat{\lambda}(1-\hat{p}) = \dfrac{e^{\hat{\beta}_0+\hat{\beta}_1 x}}{1+e^{\hat{\gamma}_0+\hat{\gamma}_1 x}}$. The control mean is also needed for calculation of the IC level. This may be estimated directly if sufficient data exist or the model-based estimate $\hat{\mu}_C = \dfrac{e^{\hat{\beta}_0}}{1+e^{\hat{\gamma}_0}}$ may be used. Hence, in order to obtain the estimate of IC $_{100*q}$, the following equation is needed

$$1-\hat{q} = \frac{\hat{\mu}_x}{\hat{\mu}_C} = \frac{(1+e^{\hat{\gamma}_0})(e^{\hat{\beta}_1 IC_{100q}})}{1+e^{\hat{\gamma}_0+\hat{\gamma}_1 IC_{100q}}}, \text{ where IC }_{100*q} = \text{x.} \tag{3.11}$$

By solving this equation, the estimate of IC$_{100*q}$ can be obtained. However, because of the complexity of the equation, it has to be solved by iterated root search methods.

Confidence intervals for the IC concentration can be obtained by using the bootstrap procedure (Efron and Tibshirani, 1993). There are two different ways of bootstrapping a regression type model. One is resampling the response and covariate pairs, and the other is resampling the residuals. Since bootstrapping the response and covariate pairs is less sensitive to the assumptions of the regression model than bootstrapping residuals (Efron and Tibshirani, 1993), the bootstrapping response and covariate pairs method is used.

For demonstration purpose, only the confidence interval of the simplest single toxicant ZIP models shown in Table 3.3 are calculated. The models in Table 3.3 are each re-fitted 2000 times along with the IC concentrations calculation using this bootstrapping techniques. Each bootstrap observations set is sampled from the original observations. In order to maintain the design structure of the original experiment, each treatment is re-sampled with 20 replications as in the original experiment.

Three IC concentration levels (IC_{10}, IC_{50}, IC_{90} in mg/l) for the two best mixture models (copper model and mercury model) are obtained by the uniroot function in S-plus which use the Newton search method. The confidence intervals of the estimated IC levels are then obtained based on the percentile method of the bootstrap technique using 2000 samples. The bootstrap results are presented in Table 3.5. The IC_{50} for the mercury model is 6.307 with 95% CI (5.897, 6.712) and the IC_{50} for the copper model is 9.959 with 95% CI (8.241, 11.579).

Table 3.11. Estimates and confidence intervals for parameters on inhibition concentrations based on 2000 bootstrap samples. Confidence intervals are based on the percentile method.

A. Mercury (unit for IC is mg/l)

	β_0	β_1	γ_0	γ_1	IC_{10}	IC_{50}	IC_{90}
estimate	2.960 (0.0124)	-0.060 (0.0035)	-1.985 (0.1496)	0.222 (0.0243)	1.169	6.307	14.795
mean	2.969	-0.060	-1.988	0.223	1.172	6.317	14.824
median	2.960	-0.060	-1.979	0.232	1.171	6.311	14.775
variance	$1.962x10^{-4}$	$1.285x10^{-5}$	$2.268x10^{-2}$	$4.627x10^{-4}$	$1.586x10^{-3}$	$4.695x10^{-2}$	$6.054x10^{-1}$
s. d.	$1.401x10^{-2}$	$3.584x10^{-3}$	$1.506x10^{-1}$	$2.151x10^{-2}$	$3.982x10^{-2}$	$2.167x10^{-1}$	$7.781x10^{-1}$
95% C.I.	(2.932, 2.989)	(-0.067, -0.053)	(-2.335, -1.736)	(0.184, 0.268)	(1.097, 1.249)	(5.897, 6.712)	(13.437, 16.290)
90% C.I.	(2.938, 2.984)	(-0.066, -0.054)	(-2.269, -1.773)	(0.189, 0.260)	(1.107, 1.239)	(5.951, 6.671)	(13.567,16.157)
80% C.I.	(2.941, 2.978)	(-0.065, -0.055)	(-2.179, -1.803)	(0.195, 0.251)	(1.120, 1.223)	(6.042, 6.597)	(13.837,15.828)

B. Copper (unit for IC is mg/l)

	β_0	β_1	γ_0	γ_1	IC_{10}	IC_{50}	IC_{90}
estimated value	2.944 (0.0142)	-0.037 (0.0036)	-1.800 (0.1231)	0.131 (0.0151)	1.826	9.959	23.886
mean	2.944	$-3.699x10^{-2}$	-1.810	$1.350x10^{-1}$	1.832	9.920	23.762
median	2.943	$-3.678x10^{-2}$	1.350	$1.327x10^{-1}$	1.831	9.889	23.760
variance	$3.734x10^{-4}$	$2.580x10^{-5}$	$1.774x10^{-2}$	$4.862x10^{-4}$	$2.479x10^{-2}$	$6.998x10^{-1}$	6.262
s. d.	0.019	0.005	0.133	0.022	0.157	0.837	2.502
95% C.I.	(2.905, 2.984)	(-0.047, -0.027)	(-2.086, -1.583)	(0.096, 0.186)	(1.534, 2.181)	(8.241, 11.579)	(18.735, 28.631)
90% C. I.	(2.913, 2.978)	(-0.046, -0.029)	(-2.028, -1.609)	(0.103, 0.174)	(1.570, 2.114)	(8.539, 11.234)	(19.573, 27.697)
80% C.I.	(2.921, 2.969)	(-0.043, -0.031)	(-1.988, -1.636)	(0.108, 0.165)	(1.645, 2.029)	(8.830, 10.959)	(20.524, 26.937)

3.8 Simulation Study

A simulation study was carried out to compare the ZIP model and Poisson model. The data were generated using a pseudo random number generator based on the zero inflated model using predetermined values of parameters. The simulation focused on the comparison of the two models, investigate how different mortality rates affect the performances of the two models. Hence, the parameters of the logistic portion, γ_0 and γ_1, are varied in order to produce different levels of mortality rate. The value of γ_0 affects the control mortality probability and the value of γ_1 affects the mortality probability with respect to the toxicant dosage level. In terms of the ZIP model, the higher the γ_0 is, the higher the mortality probability for the control. The effect of γ_1 is similar to the effect of the slope in the simple linear regression, i.e., the higher the γ_1 is, the mortality probability increases faster as the dosage increases. Three categories of mortality level were set up based on different γ_0, they are high (γ_0 = -1.5), medium (γ_0 = -3.5), low (γ_0 = -10.5). The value of γ_1 varies within the range of 0.00 to 0.14 with the increment of 0.01. The mortality probability also increases within each category as γ_1 increases. The mortality rate of the high mortality category is within the range of 18% (control) to about 80%. The mortality rate of the medium mortality category is within the range of 3% (control) to about 70%. The mortality rate of the low mortality category is within the range of 0% (control) to about 3%. On the other hand, the parameters of the Poisson portion, β_0 and β_1, are fixed at 3.5 and –0.05 respectively. These will give a average of 28% zero observations for the Poisson part and a mean control response (reproduction) of about 30 which is a reasonable number for *Ceriodaphnia* test. Figures 3.3 and 3.4 show how the responses change with the parameters.

Figure 3.3. The mortality probabilities at different values of γ_0 and γ_1
(PDF, 5K, Fig3-3.pdf)

Figure 3.4. The mean response of the Poisson part of the ZIP model at different values of β_0 and β_1. (PDF, 4K, Fig3-4.pdf)

The different lines in the figures are corresponding to different treatment level (dose) and 5 doses are shown in figures 3.3 and 3.4. Under these conditions, the model produces a fair amount of zero observations at high dosage levels and creates the problem of mixing zeroes as in the real life situations.

The data is then fitted to the zero inflated Poisson model and the regular Poisson model. The structure of the data is based on the simple toxicant model with 10 replications for each treatment and the dosages are equally divided between 0 and 100. The simulation is also designed to have 4 different number of treatment levels 3, 4, 5, 7. The low number of treatment levels is quite typical for the *Ceriodaphnia* test. Each set of simulations is then run 2000 times, and the mean estimates of the regression coefficients and the IC levels were recorded along with theirs standard deviation. They are presented in the tables (Table 3.12 - Table 3.35). The IC_{50} and the difference in the log-likelihood between the ZIP and the Poisson model of each simulation were also plotted in Figure 3.5 to Figure 3.11.

Explanation of the table

There are three categories of mortality:

1. High natural mortality: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -1.5$, $\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01
2. Median initial mortality: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -3.5$, $\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01
3. Low initial mortality: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -10.5$, $\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01

Proportion of Zeroes:

pois: the proportion of the Poisson zeroes generated in that particular run of simulation.
This can be interpreted as the proportion of zero reproduction.

bino: the proportion of the binomial zeroes generated in that particular run of simulation.
This can be interpreted as the proportion of mortality.

Total: the proportion of the total number of zeroes in that particular run of simulation.
This can be interpreted as the proportion of zero observation.

Diff. Ln(like): The difference in the log likelihood between the Poisson model and the
Zero inflated model. (ZIP minus Poisson)

The first entry of the table is the estimate or the true value and the second entry (right below the first entry) of the table is the standard deviation.

Table 3.12 - Table 3.23 show the estimates of the regression coefficients. Table 3.24 - Table 3.35 show the estimates of the IC levels (IC_{10}, IC_{50}, IC_{90}).

Table 3.12. Simulation Results
Number of treatments = 3
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -1.5$ (high natural mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson		ZIP				Proportion of Zeroes			Diff. Ln(like)
	β_0	β_1	β_0	β_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.27	-0.05	3.49	-0.05	-2.63	0.04	0.29	0.18	0.42	47.87
	0.173	0.005	0.065	0.004	2.017	0.034	0.049	0.074	0.071	29.332
0.01	3.27	-0.05	3.49	-0.05	-2.54	0.04	0.29	0.27	0.46	49.04
	0.174	0.006	0.065	0.004	2.134	0.039	0.049	0.083	0.071	29.418
0.02	3.27	-0.06	3.49	-0.05	-2.62	0.05	0.29	0.39	0.51	50.46
	0.174	0.007	0.065	0.005	2.572	0.049	0.049	0.082	0.069	29.529
0.03	3.27	-0.06	3.49	-0.05	-2.8	0.06	0.29	0.49	0.56	51.68
	0.174	0.009	0.065	0.006	2.999	0.058	0.049	0.077	0.066	29.446
0.04	3.28	-0.07	3.49	-0.05	-2.85	0.07	0.29	0.57	0.6	52.51
	0.172	0.011	0.065	0.007	3.227	0.064	0.049	0.068	0.061	29.55
0.05	3.27	-0.07	3.49	-0.05	-2.75	0.08	0.29	0.62	0.64	53.28
	0.171	0.013	0.065	0.009	3.247	0.064	0.049	0.054	0.053	29.528
0.06	3.27	-0.08	3.5	-0.05	-2.75	0.09	0.29	0.66	0.66	53.32
	0.168	0.014	0.065	0.011	3.347	0.067	0.049	0.049	0.049	29.341
0.07	3.27	-0.09	3.5	-0.05	-2.72	0.09	0.29	0.67	0.68	53.79
	0.165	0.014	0.064	0.012	3.394	0.068	0.049	0.046	0.046	29.098
0.08	3.29	-0.09	3.5	-0.05	-2.8	0.1	0.29	0.68	0.68	51.18
	0.162	0.013	0.063	0.013	3.396	0.067	0.049	0.046	0.045	28.884
0.09	3.3	-0.09	3.5	-0.05	-3.14	0.1	0.29	0.68	0.68	48.92
	0.153	0.013	0.063	0.013	3.724	0.074	0.049	0.041	0.04	28.678
0.10	3.29	-0.09	3.5	-0.05	-3.18	0.11	0.29	0.69	0.69	50.78
	0.169	0.013	0.062	0.013	3.839	0.077	0.048	0.043	0.043	30.988
0.11	3.27	-0.09	3.5	-0.05	-2.71	0.1	0.29	0.69	0.69	54.2
	0.174	0.012	0.063	0.013	3.452	0.069	0.049	0.045	0.045	30.296
0.12	3.24	-0.09	3.5	-0.05	-2.43	0.09	0.29	0.7	0.7	58.72
	0.178	0.012	0.065	0.013	3.294	0.065	0.048	0.046	0.046	30.228
0.13	3.24	-0.09	3.5	-0.05	-2.40	0.09	0.29	0.71	0.71	59.27
	0.181	0.012	0.065	0.014	3.291	0.065	0.051	0.042	0.042	30.116
0.14	3.22	-0.09	3.5	-0.05	-2.68	0.1	0.29	0.71	0.71	61.02
	0.204	0.012	0.066	0.014	3.722	0.074	0.05	0.05	0.05	35.161

Table 3.13. Simulation Results
Number of treatments = 4
True values: b_0 = 3.5, b_1 = -0.05, γ_0 = -1.5 (high natural mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson		ZIP				proportion of zeroes			Diff. Ln(like)
	b_0	b_1	b_0	b_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.27	-0.05	3.48	-0.05	-2.38	0.04	0.28	0.18	0.41	52.24
	0.17	0.005	0.064	0.003	1.277	0.019	0.049	0.062	0.067	29.778
0.01	3.28	-0.05	3.49	-0.05	-2.22	0.04	0.28	0.27	0.45	54.68
	0.17	0.006	0.065	0.003	1.205	0.018	0.049	0.071	0.068	29.945
0.02	3.28	-0.06	3.49	-0.05	-2.08	0.04	0.28	0.39	0.51	57.47
	0.171	0.007	0.065	0.004	0.896	0.015	0.049	0.071	0.065	29.873
0.03	3.28	-0.06	3.49	-0.05	-2	0.05	0.28	0.5	0.56	60.4
	0.171	0.008	0.065	0.004	1.092	0.027	0.049	0.065	0.062	30.022
0.04	3.28	-0.07	3.49	-0.05	-2.08	0.06	0.28	0.58	0.61	62.8
	0.17	0.01	0.065	0.005	1.672	0.047	0.049	0.063	0.057	30.109
0.05	3.28	-0.07	3.49	-0.05	-2.35	0.08	0.28	0.64	0.65	64.49
	0.172	0.011	0.065	0.006	2.448	0.071	0.049	0.06	0.055	30.478
0.06	3.28	-0.08	3.49	-0.05	-2.51	0.09	0.28	0.68	0.68	65.08
	0.173	0.013	0.065	0.006	2.841	0.085	0.049	0.052	0.049	30.546
0.07	3.28	-0.08	3.49	-0.05	-2.67	0.11	0.28	0.71	0.71	64.82
	0.171	0.016	0.065	0.008	3.131	0.094	0.049	0.045	0.044	30.555
0.08	3.28	-0.09	3.5	-0.05	-2.68	0.12	0.28	0.73	0.73	64.54
	0.167	0.017	0.065	0.009	3.252	0.097	0.049	0.039	0.04	30.146
0.09	3.28	-0.1	3.5	-0.05	-2.71	0.13	0.28	0.74	0.74	64.05
	0.167	0.018	0.065	0.011	3.316	0.1	0.049	0.037	0.037	30.237
0.10	3.27	-0.1	3.5	-0.05	-2.68	0.13	0.28	0.75	0.75	64.23
	0.17	0.018	0.065	0.011	3.365	0.102	0.049	0.035	0.035	30.562
0.11	3.28	-0.11	3.5	-0.05	-2.86	0.14	0.28	0.76	0.76	61.99
	0.166	0.017	0.063	0.012	3.528	0.105	0.05	0.035	0.035	30.01
0.12	3.28	-0.11	3.5	-0.05	-2.78	0.14	0.28	0.76	0.76	60.76
	0.163	0.016	0.063	0.013	3.415	0.102	0.049	0.035	0.035	29.428
0.13	3.29	-0.11	3.5	-0.05	-3.13	0.16	0.28	0.76	0.76	58.71
	0.165	0.016	0.063	0.013	3.746	0.111	0.049	0.033	0.033	30.162
0.14	3.3	-0.11	3.5	-0.05	-3	0.15	0.28	0.76	0.76	58.74
	0.154	0.015	0.062	0.014	3.606	0.107	0.049	0.03	0.03	29.178

Table 3.14. Simulation Results
Number of treatments = 5
True values: b_0 = 3.5, b_1 = -0.05, γ_0 = -1.5 (high natural mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson		ZIP				zeroes			Diff. Ln(like)
	b_0	b_1	b_0	b_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.28	-0.05	3.48	-0.05	-2.42	0.04	0.27	0.18	0.4	57.9
	0.162	0.005	0.063	0.003	0.917	0.013	0.041	0.054	0.058	30.6
0.01	3.28	-0.05	3.48	-0.05	-2.23	0.04	0.27	0.27	0.45	61.59
	0.164	0.005	0.064	0.003	0.831	0.013	0.041	0.058	0.057	30.812
0.02	3.28	-0.06	3.49	-0.05	-2.08	0.04	0.27	0.39	0.5	65.99
	0.164	0.006	0.064	0.003	0.777	0.013	0.041	0.064	0.057	30.705
0.03	3.29	-0.06	3.49	-0.05	-1.97	0.05	0.27	0.49	0.56	70.21
	0.164	0.007	0.064	0.004	0.748	0.014	0.041	0.063	0.055	30.641
0.04	3.29	-0.06	3.49	-0.05	-1.88	0.05	0.27	0.58	0.62	74.39
	0.166	0.009	0.064	0.004	0.761	0.018	0.041	0.054	0.051	30.998
0.05	3.29	-0.07	3.49	-0.05	-1.86	0.07	0.27	0.64	0.66	77.21
	0.165	0.01	0.065	0.005	1.025	0.034	0.041	0.053	0.05	30.929
0.06	3.29	-0.08	3.49	-0.05	-1.98	0.08	0.27	0.68	0.69	78.87
	0.167	0.012	0.065	0.005	1.611	0.062	0.041	0.051	0.048	31.197
0.07	3.29	-0.08	3.49	-0.05	-2.14	0.1	0.27	0.72	0.72	79.96
	0.169	0.014	0.065	0.006	2.164	0.085	0.041	0.045	0.044	31.495
0.08	3.29	-0.09	3.5	-0.05	-2.34	0.12	0.27	0.74	0.74	79.86
	0.17	0.016	0.065	0.007	2.624	0.104	0.041	0.042	0.041	31.697
0.09	3.28	-0.09	3.49	-0.05	-2.47	0.13	0.27	0.76	0.76	78.78
	0.167	0.019	0.065	0.008	2.885	0.115	0.041	0.037	0.037	31.917
0.10	3.29	-0.1	3.5	-0.05	-2.58	0.15	0.27	0.77	0.77	77.57
	0.163	0.021	0.064	0.009	3.037	0.121	0.041	0.032	0.032	32.178
0.11	3.28	-0.11	3.5	-0.05	-2.61	0.16	0.27	0.79	0.79	76.48
	0.172	0.022	0.065	0.01	3.177	0.127	0.041	0.032	0.032	31.713
0.12	3.28	-0.11	3.5	-0.05	-2.68	0.17	0.27	0.79	0.79	74.9
	0.167	0.022	0.065	0.011	3.275	0.132	0.041	0.03	0.03	31.664
0.13	3.27	-0.12	3.5	-0.05	-2.61	0.17	0.27	0.8	0.8	74.77
	0.166	0.022	0.064	0.011	3.261	0.133	0.042	0.028	0.028	31.748
0.14	3.27	-0.12	3.5	-0.05	-2.65	0.18	0.27	0.8	0.8	73.65
	0.167	0.022	0.064	0.012	3.324	0.134	0.041	0.028	0.028	31.047

Table 3.15. Simulation Results
Number of treatments = 7
True values: b_0 = 3.5, b_1 = -0.05, γ_0 = -1.5 (high natural mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson		ZIP				Proportion of zeroes			Diff. Ln(like)
	b_0	b_1	b_0	b_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.28	-0.05	3.47	-0.05	-2.42	0.04	0.25	0.18	0.39	70.09
	0.148	0.004	0.059	0.003	0.758	0.011	0.036	0.046	0.049	32.361
0.01	3.28	-0.05	3.48	-0.05	-2.2	0.04	0.25	0.27	0.44	76.49
	0.15	0.005	0.06	0.003	0.678	0.01	0.036	0.054	0.05	32.8
0.02	3.29	-0.06	3.48	-0.05	-2.06	0.04	0.25	0.39	0.5	83.08
	0.151	0.005	0.06	0.003	0.634	0.01	0.036	0.054	0.049	33.003
0.03	3.29	-0.06	3.49	-0.05	-1.95	0.05	0.25	0.5	0.56	90.34
	0.152	0.006	0.061	0.003	0.621	0.011	0.036	0.049	0.047	32.648
0.04	3.3	-0.06	3.49	-0.05	-1.86	0.05	0.25	0.58	0.62	96.42
	0.154	0.007	0.062	0.004	0.63	0.013	0.036	0.046	0.045	32.609
0.05	3.3	-0.07	3.49	-0.05	-1.79	0.06	0.25	0.65	0.67	101.63
	0.157	0.009	0.062	0.004	0.641	0.015	0.036	0.045	0.043	32.873
0.06	3.31	-0.08	3.49	-0.05	-1.74	0.07	0.25	0.69	0.7	105.21
	0.157	0.01	0.063	0.005	0.619	0.017	0.036	0.04	0.039	32.618
0.07	3.31	-0.08	3.49	-0.05	-1.72	0.08	0.25	0.73	0.73	107.34
	0.157	0.011	0.064	0.005	0.688	0.025	0.036	0.038	0.038	32.315
0.08	3.31	-0.09	3.49	-0.05	-1.74	0.09	0.25	0.75	0.76	108.23
	0.157	0.013	0.064	0.006	0.897	0.044	0.036	0.036	0.036	32.342
0.09	3.31	-0.09	3.49	-0.05	-1.82	0.11	0.25	0.77	0.78	108.02
	0.161	0.015	0.064	0.007	1.162	0.064	0.036	0.036	0.036	32.637
0.10	3.3	-0.1	3.49	-0.05	-1.95	0.13	0.25	0.79	0.79	107.48
	0.164	0.017	0.064	0.007	1.511	0.086	0.036	0.034	0.034	32.619
0.11	3.3	-0.1	3.49	-0.05	-1.93	0.14	0.25	0.8	0.8	106.47
	0.165	0.019	0.065	0.008	1.508	0.089	0.036	0.031	0.031	32.77
0.12	3.3	-0.11	3.49	-0.05	-2.05	0.16	0.25	0.81	0.81	105.12
	0.166	0.021	0.065	0.008	1.804	0.107	0.036	0.03	0.03	33.108
0.13	3.3	-0.12	3.49	-0.05	-2.11	0.17	0.25	0.82	0.82	103.34
	0.161	0.023	0.064	0.009	1.924	0.116	0.036	0.027	0.027	33.558
0.14	3.29	-0.12	3.49	-0.05	-2.23	0.19	0.25	0.83	0.83	100.6
	0.166	0.027	0.065	0.01	2.095	0.127	0.036	0.026	0.026	34.172

Table 3.16. Simulation Results
Number of treatments = 3
True values: b_0 = 3.5, b_1 = -0.05, γ_0 = -3.5 (median initial mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson		ZIP				Proportion of zeroes			Diff. Ln(like)
	b_0	b_1	b_0	b_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.45	-0.05	3.49	-0.05	-5.2	0.07	0.3	0.04	0.33	11.94
	0.082	0.004	0.058	0.004	2.955	0.055	0.049	0.033	0.05	15.55
0.01	3.45	-0.05	3.49	-0.05	-5.3	0.07	0.29	0.06	0.33	11.52
	0.082	0.004	0.059	0.004	3.121	0.058	0.05	0.039	0.051	15.42
0.02	3.45	-0.05	3.49	-0.05	-5.58	0.08	0.29	0.1	0.34	10.74
	0.082	0.004	0.06	0.004	3.452	0.065	0.049	0.051	0.051	15.178
0.03	3.46	-0.05	3.49	-0.05	-6.06	0.09	0.29	0.18	0.37	10.62
	0.081	0.004	0.059	0.004	4.001	0.076	0.049	0.065	0.052	14.965
0.04	3.46	-0.05	3.5	-0.05	-7.09	0.12	0.29	0.28	0.4	10.75
	0.081	0.005	0.059	0.004	4.583	0.087	0.049	0.069	0.053	14.748
0.05	3.46	-0.06	3.5	-0.05	-8.11	0.15	0.29	0.37	0.44	11.63
	0.08	0.006	0.059	0.005	4.709	0.09	0.049	0.066	0.054	14.578
0.06	3.46	-0.06	3.5	-0.05	-8.39	0.16	0.29	0.44	0.48	12.59
	0.08	0.007	0.059	0.005	4.411	0.085	0.049	0.063	0.054	14.692
0.07	3.46	-0.07	3.5	-0.05	-8.41	0.17	0.29	0.49	0.51	13.4
	0.08	0.009	0.059	0.006	4.137	0.081	0.049	0.061	0.054	14.818
0.08	3.46	-0.07	3.5	-0.05	-8.3	0.18	0.29	0.54	0.55	14.01
	0.08	0.011	0.059	0.007	4.019	0.08	0.049	0.052	0.049	14.956
0.09	3.46	-0.08	3.5	-0.05	-8.27	0.19	0.29	0.58	0.59	14.25
	0.08	0.012	0.059	0.009	4.078	0.082	0.049	0.041	0.041	15.196
0.10	3.46	-0.08	3.5	-0.05	-8.36	0.2	0.29	0.61	0.61	14.03
	0.08	0.014	0.059	0.011	4.164	0.084	0.049	0.037	0.036	15.265
0.11	3.46	-0.09	3.5	-0.05	-8.6	0.21	0.29	0.62	0.62	13.34
	0.08	0.013	0.059	0.012	4.137	0.084	0.049	0.031	0.03	15.31
0.12	3.47	-0.09	3.5	-0.05	-8.78	0.21	0.29	0.63	0.63	12.84
	0.08	0.013	0.058	0.013	4.094	0.082	0.049	0.027	0.026	15.471
0.13	3.47	-0.09	3.5	-0.05	-9.2	0.22	0.28	0.63	0.63	11.58
	0.078	0.013	0.058	0.013	3.856	0.079	0.049	0.02	0.02	15.155
0.14	3.46	-0.09	3.5	-0.05	-8.74	0.22	0.29	0.64	0.64	12.99
	0.081	0.012	0.056	0.014	4.112	0.084	0.048	0.02	0.02	16.138

Table 3.17. Simulation Results
Number of treatments = 4
True values: β_0 = 3.5, β_1 = -0.05, γ_0 = -3.5 (median initial mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson		ZIP				Proportion of zeroes			Diff. Ln(like)
	β_0	β_1	β_0	β_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.46	-0.05	3.49	-0.05	-6.38	0.08	0.28	0.03	0.3	8.33
	0.078	0.003	0.058	0.003	4.974	0.073	0.049	0.028	0.053	14.727
0.01	3.46	-0.05	3.49	-0.05	-6.12	0.08	0.28	0.05	0.31	8.76
	0.078	0.003	0.058	0.003	4.79	0.07	0.049	0.034	0.054	14.85
0.02	3.46	-0.05	3.49	-0.05	-5.83	0.08	0.28	0.09	0.33	9.41
	0.078	0.003	0.058	0.003	4.524	0.067	0.049	0.043	0.055	14.962
0.03	3.46	-0.05	3.49	-0.05	-5.91	0.08	0.28	0.16	0.35	10.61
	0.078	0.004	0.059	0.003	4.982	0.074	0.049	0.053	0.054	15.055
0.04	3.47	-0.05	3.49	-0.05	-6.45	0.1	0.28	0.26	0.39	12.37
	0.078	0.004	0.059	0.003	6.054	0.09	0.049	0.057	0.053	15.187
0.05	3.47	-0.06	3.49	-0.05	-5.68	0.1	0.28	0.36	0.44	14.56
	0.078	0.004	0.059	0.004	4.91	0.076	0.049	0.053	0.052	15.309
0.06	3.47	-0.06	3.49	-0.05	-5.46	0.1	0.28	0.43	0.48	17
	0.078	0.005	0.059	0.004	4.495	0.08	0.049	0.057	0.051	15.441
0.07	3.47	-0.06	3.5	-0.05	-5.51	0.12	0.28	0.5	0.52	19.59
	0.078	0.006	0.059	0.004	4.09	0.096	0.049	0.052	0.048	15.425
0.08	3.47	-0.07	3.5	-0.05	-6.29	0.16	0.28	0.54	0.56	21.81
	0.078	0.007	0.059	0.005	4.396	0.121	0.049	0.05	0.047	15.407
0.09	3.47	-0.07	3.5	-0.05	-6.86	0.19	0.28	0.58	0.59	23.79
	0.078	0.008	0.059	0.005	4.406	0.129	0.049	0.047	0.045	15.478
0.10	3.47	-0.07	3.5	-0.05	-7.55	0.22	0.28	0.61	0.61	25.15
	0.079	0.01	0.059	0.006	4.38	0.129	0.049	0.049	0.046	15.459
0.11	3.47	-0.08	3.5	-0.05	-7.96	0.24	0.28	0.63	0.64	26.11
	0.079	0.011	0.059	0.006	4.243	0.126	0.049	0.043	0.042	15.528
0.12	3.47	-0.08	3.5	-0.05	-8.16	0.26	0.28	0.66	0.66	26.4
	0.079	0.013	0.059	0.007	4.111	0.124	0.049	0.039	0.038	15.667
0.13	3.46	-0.09	3.5	-0.05	-8.06	0.27	0.28	0.68	0.68	26.1
	0.08	0.016	0.059	0.008	4.144	0.127	0.049	0.034	0.034	16.39
0.14	3.46	-0.1	3.5	-0.05	-8.23	0.28	0.28	0.7	0.7	25.5
	0.08	0.016	0.059	0.01	4.151	0.124	0.049	0.031	0.031	16.051

Table 3.18. Simulation Results
Number of treatments = 5
True values: b_0 = 3.5, b_1 = -0.05, γ_0 = -3.5 (median initial mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson		ZIP				Proportion of zeroes			Diff. Ln(like)
	b_0	b_1	b_0	b_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.46	-0.05	3.48	-0.05	-6.31	0.08	0.27	0.03	0.29	8.56
	0.075	0.003	0.057	0.003	4.928	0.065	0.041	0.027	0.046	15.107
0.01	3.46	-0.05	3.48	-0.05	-5.79	0.08	0.27	0.05	0.3	9.31
	0.075	0.003	0.057	0.003	4.039	0.053	0.041	0.032	0.047	15.189
0.02	3.46	-0.05	3.49	-0.05	-5.63	0.08	0.27	0.09	0.32	10.2
	0.076	0.003	0.058	0.003	4.215	0.057	0.041	0.038	0.047	15.405
0.03	3.47	-0.05	3.49	-0.05	-5.42	0.08	0.27	0.16	0.34	11.77
	0.076	0.003	0.058	0.003	4.152	0.056	0.041	0.047	0.047	15.584
0.04	3.47	-0.05	3.49	-0.05	-5.02	0.08	0.27	0.25	0.39	14.32
	0.076	0.003	0.058	0.003	3.096	0.045	0.041	0.05	0.047	15.862
0.05	3.48	-0.06	3.49	-0.05	-4.96	0.08	0.27	0.35	0.43	17.31
	0.076	0.004	0.058	0.003	3.387	0.055	0.041	0.052	0.045	16.001
0.06	3.48	-0.06	3.49	-0.05	-5.52	0.11	0.27	0.43	0.48	21.01
	0.077	0.004	0.058	0.003	4.959	0.095	0.041	0.046	0.043	16.301
0.07	3.49	-0.06	3.5	-0.05	-5.02	0.11	0.27	0.5	0.52	24.53
	0.076	0.005	0.058	0.004	4.016	0.08	0.041	0.045	0.044	16.496
0.08	3.49	-0.06	3.5	-0.05	-5	0.12	0.27	0.55	0.56	27.97
	0.077	0.006	0.058	0.004	4.1	0.089	0.041	0.045	0.043	16.653
0.09	3.49	-0.07	3.5	-0.05	-5	0.13	0.27	0.59	0.59	31.13
	0.076	0.006	0.059	0.004	3.976	0.102	0.041	0.045	0.043	16.489
0.10	3.49	-0.07	3.5	-0.05	-5.11	0.15	0.27	0.62	0.62	33.95
	0.076	0.007	0.059	0.005	3.762	0.124	0.041	0.04	0.039	16.487
0.11	3.49	-0.07	3.5	-0.05	-5.79	0.19	0.27	0.64	0.64	35.97
	0.076	0.008	0.059	0.005	4.233	0.155	0.041	0.039	0.039	16.366
0.12	3.48	-0.08	3.5	-0.05	-6.39	0.23	0.27	0.66	0.66	38.09
	0.077	0.009	0.059	0.006	4.395	0.171	0.041	0.038	0.038	16.57
0.13	3.48	-0.08	3.5	-0.05	-6.81	0.26	0.27	0.68	0.68	39.46
	0.077	0.011	0.059	0.006	4.433	0.176	0.042	0.039	0.038	16.912
0.14	3.48	-0.09	3.5	-0.05	-7.76	0.31	0.27	0.7	0.7	40.05
	0.078	0.013	0.059	0.006	4.462	0.176	0.041	0.037	0.037	16.32

Table 3.19. Simulation Results
Number of treatments = 7
True values: $b_0 = 3.5$, $b_1 = -0.05$, $\gamma_0 = -3.5$ (median initial mortality),
$\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01

γ_1	Poisson		ZIP				Proportion of zeroes			Diff. Ln(like)
	b_0	b_1	b_0	b_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.46	-0.05	3.47	-0.05	-5.57	0.07	0.25	0.03	0.27	9.19
	0.07	0.003	0.054	0.002	1.828	0.024	0.036	0.022	0.04	15.957
0.01	3.46	-0.05	3.48	-0.05	-5.27	0.07	0.25	0.05	0.29	10.38
	0.071	0.003	0.054	0.002	1.648	0.022	0.036	0.027	0.04	16.27
0.02	3.46	-0.05	3.48	-0.05	-5.03	0.07	0.25	0.09	0.3	11.93
	0.071	0.003	0.054	0.002	1.58	0.021	0.036	0.033	0.04	16.418
0.03	3.47	-0.05	3.48	-0.05	-4.81	0.07	0.25	0.16	0.33	14.17
	0.071	0.003	0.054	0.002	1.551	0.022	0.036	0.04	0.04	16.667
0.04	3.48	-0.05	3.48	-0.05	-4.6	0.07	0.25	0.25	0.38	17.87
	0.072	0.003	0.055	0.003	1.287	0.019	0.036	0.043	0.039	17.193
0.05	3.49	-0.06	3.49	-0.05	-4.53	0.08	0.25	0.35	0.43	22.29
	0.072	0.003	0.055	0.003	1.577	0.025	0.036	0.043	0.037	17.329
0.06	3.49	-0.06	3.49	-0.05	-4.37	0.08	0.25	0.43	0.48	27.9
	0.073	0.004	0.056	0.003	1.401	0.025	0.036	0.041	0.038	17.892
0.07	3.5	-0.06	3.49	-0.05	-4.25	0.09	0.25	0.5	0.52	33.36
	0.073	0.004	0.056	0.003	1.482	0.029	0.036	0.039	0.038	18.316
0.08	3.51	-0.07	3.49	-0.05	-4.21	0.1	0.25	0.55	0.56	38.54
	0.074	0.005	0.056	0.004	1.768	0.039	0.036	0.039	0.036	18.649
0.09	3.51	-0.07	3.5	-0.05	-4.43	0.12	0.25	0.59	0.6	43.65
	0.075	0.005	0.057	0.004	2.867	0.076	0.036	0.034	0.033	18.586
0.10	3.51	-0.07	3.5	-0.05	-4.16	0.12	0.25	0.63	0.63	48.06
	0.074	0.005	0.057	0.004	1.928	0.054	0.036	0.032	0.031	18.553
0.11	3.52	-0.08	3.5	-0.05	-4.33	0.14	0.25	0.65	0.66	51.37
	0.075	0.006	0.057	0.005	2.392	0.071	0.036	0.032	0.032	18.584
0.12	3.52	-0.08	3.5	-0.05	-4.32	0.15	0.25	0.68	0.68	54.38
	0.075	0.007	0.058	0.005	2.428	0.08	0.036	0.032	0.032	18.511
0.13	3.52	-0.08	3.5	-0.05	-4.41	0.16	0.25	0.69	0.7	56.82
	0.075	0.008	0.058	0.005	2.56	0.095	0.036	0.033	0.033	18.342
0.14	3.52	-0.09	3.5	-0.05	-4.44	0.18	0.25	0.71	0.71	58.78
	0.075	0.008	0.058	0.005	2.529	0.1	0.036	0.03	0.03	18.068

Table 3.20. Simulation Results
Number of treatments = 3
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -10.5$ (low natural mortality),
$\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01

γ_1	Poisson		ZIP				Proportion of Zeroes			Diff. Ln(like)
	b_0	b_1	b_0	b_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.5	-0.05	3.5	-0.05	-6.53	0.09	0.31	0	0.31	-0.85
	0.056	0.004	0.056	0.004	3.158	0.062	0.045	0	0.045	1.534
0.01	3.5	-0.05	3.5	-0.05	-6.53	0.09	0.31	0	0.31	-0.85
	0.056	0.004	0.056	0.004	3.158	0.062	0.045	0	0.045	1.534
0.02	3.5	-0.05	3.5	-0.05	-6.53	0.09	0.31	0	0.31	-0.85
	0.056	0.004	0.056	0.004	3.158	0.062	0.045	0	0.045	1.534
0.03	3.5	-0.05	3.5	-0.05	-6.53	0.09	0.31	0	0.31	-0.85
	0.056	0.004	0.056	0.004	3.158	0.062	0.045	0.003	0.045	1.534
0.04	3.5	-0.05	3.5	-0.05	-6.54	0.09	0.31	0	0.31	-0.85
	0.055	0.004	0.056	0.004	3.171	0.062	0.045	0.004	0.045	1.537
0.05	3.5	-0.05	3.5	-0.05	-6.56	0.09	0.31	0	0.31	-0.84
	0.055	0.004	0.056	0.004	3.197	0.063	0.045	0.007	0.045	1.541
0.06	3.5	-0.05	3.5	-0.05	-6.58	0.09	0.31	0	0.31	-0.83
	0.055	0.004	0.056	0.004	3.224	0.063	0.045	0.011	0.045	1.544
0.07	3.5	-0.05	3.5	-0.05	-6.63	0.09	0.31	0.01	0.31	-0.79
	0.055	0.004	0.056	0.004	3.254	0.064	0.045	0.019	0.045	1.555
0.08	3.5	-0.05	3.5	-0.05	-6.84	0.1	0.31	0.03	0.32	-0.68
	0.055	0.004	0.056	0.004	3.424	0.067	0.045	0.03	0.044	1.603
0.09	3.5	-0.05	3.5	-0.05	-7.24	0.1	0.31	0.06	0.32	-0.51
	0.055	0.004	0.055	0.004	3.714	0.073	0.045	0.043	0.042	1.648
0.10	3.5	-0.05	3.5	-0.05	-8.16	0.12	0.31	0.13	0.34	-0.09
	0.055	0.004	0.055	0.004	4.21	0.083	0.046	0.051	0.038	1.723
0.11	3.5	-0.05	3.5	-0.05	-10.11	0.16	0.31	0.21	0.35	0.59
	0.055	0.004	0.056	0.004	4.684	0.093	0.046	0.052	0.034	1.749
0.12	3.5	-0.05	3.5	-0.05	-12.24	0.21	0.31	0.28	0.37	1.28
	0.055	0.004	0.056	0.004	4.296	0.085	0.047	0.044	0.029	1.663
0.13	3.5	-0.05	3.5	-0.05	-13.73	0.24	0.3	0.32	0.38	1.75
	0.054	0.004	0.055	0.004	3.327	0.065	0.048	0.036	0.025	1.489
0.14	3.5	-0.05	3.5	-0.05	-14.44	0.25	0.3	0.34	0.38	1.99
	0.056	0.004	0.056	0.004	2.282	0.042	0.048	0.028	0.025	1.343

Table 3.21. Simulation Results
Number of treatments = 4
True values: b_0 = 3.5, b_1 = -0.05, γ_0 = -10.5 (low natural mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson		ZIP				Proportion of zeroes			Diff. Ln(like)
	b_0	b_1	b_0	b_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.5	-0.05	3.49	-0.05	-8.39	0.11	0.28	0	0.28	-1.58
	0.057	0.003	0.058	0.003	5.789	0.087	0.049	0	0.049	1.938
0.01	3.5	-0.05	3.49	-0.05	-8.39	0.11	0.28	0	0.28	-1.58
	0.057	0.003	0.058	0.003	5.789	0.087	0.049	0.001	0.049	1.938
0.02	3.5	-0.05	3.49	-0.05	-8.39	0.11	0.28	0	0.28	-1.58
	0.057	0.003	0.058	0.003	5.789	0.087	0.049	0.002	0.049	1.938
0.03	3.5	-0.05	3.49	-0.05	-8.39	0.11	0.28	0	0.28	-1.58
	0.057	0.003	0.058	0.003	5.788	0.087	0.049	0.002	0.049	1.938
0.04	3.5	-0.05	3.49	-0.05	-8.39	0.11	0.28	0	0.28	-1.58
	0.057	0.003	0.058	0.003	5.789	0.087	0.049	0.003	0.049	1.937
0.05	3.5	-0.05	3.49	-0.05	-8.38	0.11	0.28	0	0.28	-1.57
	0.057	0.003	0.058	0.003	5.783	0.087	0.049	0.006	0.049	1.942
0.06	3.5	-0.05	3.49	-0.05	-8.44	0.11	0.28	0	0.28	-1.56
	0.057	0.003	0.058	0.003	5.848	0.088	0.049	0.009	0.048	1.948
0.07	3.5	-0.05	3.49	-0.05	-8.56	0.11	0.28	0.01	0.28	-1.52
	0.057	0.003	0.058	0.003	5.966	0.089	0.049	0.014	0.049	1.964
0.08	3.5	-0.05	3.49	-0.05	-8.76	0.12	0.28	0.02	0.29	-1.41
	0.057	0.003	0.058	0.003	6.147	0.092	0.049	0.022	0.048	1.981
0.09	3.5	-0.05	3.49	-0.05	-9.33	0.12	0.28	0.05	0.29	-1.2
	0.057	0.003	0.057	0.003	6.598	0.099	0.049	0.03	0.047	2.008
0.10	3.5	-0.05	3.49	-0.05	-11.05	0.15	0.28	0.1	0.3	-0.68
	0.057	0.003	0.058	0.003	7.736	0.116	0.049	0.039	0.045	2.07
0.11	3.5	-0.05	3.49	-0.05	-14.29	0.2	0.28	0.16	0.32	0.15
	0.056	0.003	0.058	0.003	8.783	0.131	0.049	0.041	0.043	2.095
0.12	3.5	-0.05	3.49	-0.05	-17.71	0.26	0.28	0.22	0.33	0.99
	0.056	0.003	0.058	0.003	8.569	0.127	0.049	0.036	0.042	1.949
0.13	3.51	-0.05	3.49	-0.05	-20.1	0.29	0.28	0.26	0.35	1.65
	0.057	0.003	0.058	0.003	7.205	0.106	0.048	0.037	0.042	1.825
0.14	3.51	-0.05	3.49	-0.05	-20.99	0.31	0.28	0.3	0.37	2.18
	0.056	0.003	0.058	0.003	6.202	0.094	0.049	0.039	0.042	1.913

Table 3.22. Simulation Results
Number of treatments = 5
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -10.5$ (low natural mortality),
$\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01

γ_1	Poisson		ZIP				proportion of zeroes			Diff. Ln(like)
	β_0	β_1	β_0	β_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.5	-0.05	3.48	-0.05	-8.67	0.11	0.27	0	0.27	-2.15
	0.056	0.002	0.057	0.003	6.662	0.089	0.041	0.001	0.041	1.823
0.01	3.5	-0.05	3.48	-0.05	-8.67	0.11	0.27	0	0.27	-2.15
	0.056	0.002	0.057	0.003	6.662	0.089	0.041	0.001	0.041	1.823
0.02	3.5	-0.05	3.48	-0.05	-8.67	0.11	0.27	0	0.27	-2.15
	0.056	0.002	0.057	0.003	6.662	0.089	0.041	0.002	0.041	1.823
0.03	3.5	-0.05	3.48	-0.05	-8.67	0.11	0.27	0	0.27	-2.15
	0.056	0.002	0.057	0.003	6.662	0.089	0.041	0.002	0.041	1.823
0.04	3.5	-0.05	3.48	-0.05	-8.67	0.11	0.27	0	0.27	-2.14
	0.056	0.002	0.057	0.003	6.663	0.089	0.041	0.002	0.041	1.825
0.05	3.5	-0.05	3.48	-0.05	-8.66	0.11	0.27	0	0.27	-2.14
	0.056	0.002	0.057	0.003	6.636	0.089	0.041	0.004	0.041	1.824
0.06	3.5	-0.05	3.48	-0.05	-8.69	0.11	0.27	0	0.27	-2.12
	0.056	0.002	0.057	0.003	6.687	0.089	0.041	0.007	0.041	1.825
0.07	3.5	-0.05	3.48	-0.05	-8.79	0.11	0.27	0.01	0.27	-2.07
	0.055	0.002	0.057	0.003	6.847	0.092	0.041	0.012	0.041	1.853
0.08	3.5	-0.05	3.48	-0.05	-9.04	0.12	0.27	0.02	0.27	-1.96
	0.055	0.002	0.057	0.003	7.192	0.096	0.041	0.016	0.041	1.881
0.09	3.5	-0.05	3.48	-0.05	-9.7	0.13	0.27	0.04	0.28	-1.68
	0.056	0.002	0.057	0.003	8.024	0.107	0.041	0.024	0.04	1.959
0.10	3.5	-0.05	3.49	-0.05	-11.09	0.15	0.27	0.08	0.29	-1.15
	0.056	0.003	0.057	0.003	9.472	0.126	0.041	0.032	0.039	2.033
0.11	3.5	-0.05	3.49	-0.05	-13.8	0.18	0.27	0.14	0.3	-0.21
	0.055	0.003	0.057	0.003	11.909	0.163	0.041	0.034	0.038	2.186
0.12	3.51	-0.05	3.49	-0.05	-16.29	0.22	0.27	0.2	0.32	0.73
	0.055	0.003	0.057	0.003	12.885	0.174	0.041	0.033	0.036	2.159
0.13	3.51	-0.05	3.49	-0.05	-18.38	0.26	0.27	0.25	0.34	1.85
	0.055	0.003	0.057	0.003	14.547	0.206	0.042	0.031	0.034	2.165
0.14	3.52	-0.05	3.49	-0.05	-19.88	0.29	0.27	0.3	0.36	3.05
	0.055	0.003	0.057	0.003	16.614	0.244	0.042	0.032	0.032	2.367

Table 3.23. Simulation Results
Number of treatments = 7
True values: β_0 = 3.5, β_1 = -0.05, γ_0 = -10.5 (low natural mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson		ZIP				Proportion of zeroes			Diff. Ln(like)
	β_0	β_1	β_0	β_1	γ_0	γ_1	pois.	bino.	Total	
0.00	3.49	-0.05	3.47	-0.05	-7.33	0.09	0.25	0	0.25	-3.35
	0.052	0.002	0.053	0.002	2.392	0.03	0.036	0.001	0.036	2.021
0.01	3.49	-0.05	3.47	-0.05	-7.34	0.09	0.25	0	0.25	-3.36
	0.052	0.002	0.053	0.002	2.275	0.029	0.036	0	0.036	1.993
0.02	3.49	-0.05	3.47	-0.05	-7.33	0.09	0.25	0	0.25	-3.35
	0.052	0.002	0.053	0.002	2.391	0.03	0.036	0.001	0.036	2.021
0.03	3.49	-0.05	3.47	-0.05	-7.33	0.09	0.25	0	0.25	-3.35
	0.052	0.002	0.053	0.002	2.393	0.03	0.036	0.002	0.036	2.022
0.04	3.49	-0.05	3.47	-0.05	-7.33	0.09	0.25	0	0.25	-3.35
	0.052	0.002	0.053	0.002	2.393	0.03	0.036	0.003	0.036	2.023
0.05	3.49	-0.05	3.47	-0.05	-7.33	0.09	0.25	0	0.25	-3.35
	0.052	0.002	0.053	0.002	2.393	0.03	0.036	0.002	0.036	2.022
0.06	3.49	-0.05	3.47	-0.05	-7.35	0.09	0.25	0	0.25	-3.32
	0.052	0.002	0.053	0.002	2.279	0.029	0.036	0.006	0.036	2.009
0.07	3.49	-0.05	3.47	-0.05	-7.37	0.09	0.25	0.01	0.25	-3.28
	0.052	0.002	0.053	0.002	2.296	0.03	0.036	0.009	0.036	2.037
0.08	3.5	-0.05	3.48	-0.05	-7.46	0.09	0.25	0.01	0.26	-3.15
	0.052	0.002	0.053	0.002	2.306	0.03	0.036	0.014	0.036	2.08
0.09	3.5	-0.05	3.48	-0.05	-7.58	0.1	0.25	0.03	0.26	-2.86
	0.052	0.002	0.053	0.002	2.07	0.027	0.036	0.022	0.035	2.125
0.10	3.5	-0.05	3.48	-0.05	-8.07	0.1	0.25	0.07	0.27	-2.2
	0.052	0.002	0.053	0.002	2.913	0.038	0.036	0.026	0.034	2.299
0.11	3.5	-0.05	3.48	-0.05	-8.76	0.12	0.25	0.13	0.29	-1.16
	0.052	0.002	0.054	0.002	3.564	0.047	0.036	0.03	0.033	2.382
0.12	3.51	-0.05	3.48	-0.05	-9.97	0.14	0.25	0.19	0.31	0.36
	0.052	0.002	0.054	0.002	5.112	0.073	0.036	0.034	0.032	2.605
0.13	3.51	-0.05	3.49	-0.05	-11.76	0.17	0.25	0.24	0.33	2.01
	0.052	0.002	0.054	0.002	7.687	0.112	0.036	0.033	0.03	2.789
0.14	3.52	-0.05	3.49	-0.05	-13.33	0.2	0.25	0.29	0.35	3.76
	0.052	0.002	0.054	0.003	9.137	0.136	0.036	0.029	0.029	2.913

Table 3.24. Simulation Results
Number of treatments = 3
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -1.5$ (high natural mortality),
$\gamma_1 = (0.00$ to $0.14)$ by 0.01

γ_1	Poisson			ZIP			True values		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.85	14.1	2.14	43.35	13.63	2.09	46.05	13.86	2.11
	5.15	1.55	0.24	3.66	1.16	0.18			
0.01	44.75	13.47	2.05	42.07	13.33	2.05	44.12	13.35	2.03
	5.3	1.59	0.24	3.74	1.23	0.19			
0.02	41.78	12.58	1.91	40.2	12.9	1.99	41.78	12.82	1.96
	5.41	1.63	0.25	3.91	1.34	0.21			
0.03	38.62	11.63	1.77	38.22	12.46	1.93	39.2	12.3	1.89
	5.55	1.67	0.25	4.15	1.5	0.23			
0.04	35.13	10.57	1.61	36.16	12	1.87	36.58	11.78	1.83
	5.5	1.66	0.25	4.51	1.74	0.27			
0.05	31.91	9.61	1.46	34.06	11.51	1.81	34.08	11.28	1.77
	5.12	1.54	0.23	4.76	1.93	0.3			
0.06	29.21	8.79	1.34	32.23	11.07	1.75	31.76	10.79	1.72
	4.87	1.47	0.22	5.1	2.19	0.35			
0.07	27.79	8.37	1.27	31.24	10.83	1.72	29.65	10.33	1.66
	4.52	1.36	0.21	5.2	2.35	0.37			
0.08	26.59	8	1.22	30.51	10.69	1.71	27.75	9.89	1.61
	3.99	1.2	0.18	5.15	2.43	0.39			
0.09	26.04	7.84	1.19	30.45	10.77	1.72	26.05	9.47	1.56
	3.75	1.13	0.17	5.3	2.65	0.42			
0.10	25.78	7.76	1.18	30.26	10.72	1.71	24.52	9.08	1.52
	3.66	1.1	0.17	5.38	2.83	0.45			
0.11	25.81	7.77	1.18	29.79	10.49	1.67	23.14	8.72	1.47
	3.45	1.04	0.16	5.1	2.61	0.42			
0.12	25.58	7.7	1.17	29.22	10.2	1.63	21.9	8.37	1.43
	3.24	0.97	0.15	4.95	2.41	0.39			
0.13	25.25	7.6	1.16	28.87	10.06	1.61	20.78	8.05	1.39
	3.44	1.03	0.16	4.9	2.4	0.39			
0.14	25.28	7.61	1.16	29.1	10.12	1.61	19.77	7.75	1.36
	3.3	0.99	0.15	5.07	2.56	0.41			

Table 3.25. Simulation Results
Number of treatments = 4
True values: $b_0 = 3.5$, $b_1 = -0.05$, $\gamma_0 = -1.5$ (high natural mortality),
$\gamma_1 = (0.00$ to $0.14)$ by 0.01

γ_1	Poisson			ZIP			True		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.92	14.12	2.15	43.36	13.64	2.1	46.05	13.86	2.11
	5	1.51	0.23	3.05	0.97	0.15			
0.01	44.88	13.51	2.05	42.03	13.32	2.05	44.12	13.35	2.03
	5	1.51	0.23	3.08	0.99	0.15			
0.02	42.17	12.69	1.93	40.06	12.88	1.99	41.78	12.82	1.96
	5.13	1.55	0.23	3.11	1.02	0.16			
0.03	39.06	11.76	1.79	37.73	12.36	1.93	39.2	12.3	1.89
	5.16	1.55	0.24	3.22	1.1	0.17			
0.04	36.13	10.88	1.65	35.37	11.88	1.87	36.58	11.78	1.83
	5.2	1.57	0.24	3.39	1.24	0.2			
0.05	33.3	10.02	1.52	33.19	11.47	1.81	34.08	11.28	1.77
	5.05	1.52	0.23	3.48	1.44	0.22			
0.06	30.68	9.24	1.4	31.26	11.08	1.76	31.76	10.79	1.72
	5.04	1.52	0.23	3.42	1.6	0.25			
0.07	28.13	8.47	1.29	29.38	10.69	1.72	29.65	10.33	1.66
	4.89	1.47	0.22	3.59	1.81	0.28			
0.08	25.84	7.78	1.18	27.78	10.3	1.67	27.75	9.89	1.61
	4.51	1.36	0.21	3.58	1.96	0.31			
0.09	24.36	7.33	1.11	26.58	10.03	1.64	26.05	9.47	1.56
	4.34	1.31	0.2	3.55	2.14	0.34			
0.10	23.36	7.03	1.07	25.9	9.84	1.61	24.52	9.08	1.52
	4.06	1.22	0.19	3.44	2.24	0.36			
0.11	22.28	6.71	1.02	25.1	9.73	1.6	23.14	8.72	1.47
	3.69	1.11	0.17	3.4	2.45	0.4			
0.12	21.61	6.51	0.99	24.62	9.58	1.59	21.9	8.37	1.43
	3.29	0.99	0.15	3.29	2.43	0.4			
0.13	21.28	6.41	0.97	24.53	9.76	1.61	20.78	8.05	1.39
	3.11	0.94	0.14	3.36	2.73	0.44			
0.14	21.08	6.35	0.96	24.28	9.61	1.6	19.77	7.75	1.36
	2.92	0.88	0.13	3.17	2.62	0.42			

Table 3.26. Simulation Results
Number of treatments = 5
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -1.5$ (high natural mortality),
$\gamma_1 = (0.00$ to $0.14)$ by 0.01

γ_1	Poisson			ZIP					
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.95	14.13	2.15	43.36	13.65	2.1	46.05	13.86	2.11
	4.74	1.43	0.22	2.61	0.83	0.13			
0.01	44.92	13.52	2.06	42.04	13.34	2.06	44.12	13.35	2.03
	4.73	1.42	0.22	2.68	0.86	0.13			
0.02	42.26	12.72	1.93	40.14	12.9	2	41.78	12.82	1.96
	4.75	1.43	0.22	2.7	0.89	0.14			
0.03	39.38	11.85	1.8	37.95	12.41	1.93	39.2	12.3	1.89
	4.87	1.47	0.22	2.8	0.94	0.15			
0.04	36.39	10.96	1.67	35.56	11.89	1.87	36.58	11.78	1.83
	4.75	1.43	0.22	2.89	1	0.16			
0.05	33.73	10.15	1.54	33.23	11.39	1.81	34.08	11.28	1.77
	4.77	1.44	0.22	3.07	1.1	0.18			
0.06	31.36	9.44	1.44	31.1	10.99	1.76	31.76	10.79	1.72
	4.79	1.44	0.22	3.32	1.27	0.21			
0.07	29.12	8.77	1.33	29.16	10.6	1.72	29.65	10.33	1.66
	4.62	1.39	0.21	3.36	1.46	0.24			
0.08	27.17	8.18	1.24	27.49	10.28	1.68	27.75	9.89	1.61
	4.73	1.42	0.22	3.42	1.65	0.27			
0.09	25.23	7.6	1.15	25.91	9.94	1.64	26.05	9.47	1.56
	4.59	1.38	0.21	3.5	1.83	0.3			
0.10	23.56	7.09	1.08	24.49	9.62	1.6	24.52	9.08	1.52
	4.38	1.32	0.2	3.38	1.96	0.32			
0.11	21.89	6.59	1	23.25	9.29	1.56	23.14	8.72	1.47
	4.11	1.24	0.19	3.26	2.11	0.35			
0.12	20.86	6.28	0.95	22.38	9.07	1.53	21.9	8.37	1.43
	3.96	1.19	0.18	3.07	2.2	0.37			
0.13	20.12	6.06	0.92	21.9	8.91	1.52	20.78	8.05	1.39
	3.71	1.12	0.17	2.97	2.21	0.40			
0.14	19.44	5.85	0.89	21.32	8.75	1.49	19.77	7.75	1.36
	3.53	1.06	0.16	2.89	2.29	0.41			

Table 3.27. Simulation Results
Number of treatments = 7
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -1.5$ (high natural mortality),
$\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01

γ_1	Poisson			ZIP					
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.77	14.08	2.14	43.33	13.63	2.1	46.05	13.86	2.11
	4.24	1.28	0.19	2.29	0.73	0.11			
0.01	44.62	13.43	2.04	41.93	13.29	2.05	44.12	13.35	2.03
	4.17	1.26	0.19	2.36	0.76	0.12			
0.02	41.99	12.64	1.92	40.06	12.85	1.99	41.78	12.82	1.96
	4	1.2	0.18	2.31	0.78	0.12			
0.03	38.94	11.72	1.78	37.74	12.33	1.92	39.2	12.3	1.89
	3.92	1.18	0.18	2.31	0.81	0.13			
0.04	36.09	10.86	1.65	35.47	11.83	1.86	36.58	11.78	1.83
	3.98	1.2	0.18	2.34	0.85	0.14			
0.05	33.39	10.05	1.53	33.18	11.31	1.79	34.08	11.28	1.77
	3.98	1.2	0.18	2.51	0.92	0.15			
0.06	31.07	9.35	1.42	31.08	10.83	1.74	31.76	10.79	1.72
	3.9	1.17	0.18	2.55	0.96	0.16			
0.07	28.99	8.73	1.33	29.09	10.38	1.68	29.65	10.33	1.66
	3.92	1.18	0.18	2.72	1.02	0.18			
0.08	27.14	8.17	1.24	27.29	9.96	1.64	27.75	9.89	1.61
	3.83	1.15	0.18	2.85	1.09	0.2			
0.09	25.53	7.69	1.17	25.62	9.6	1.6	26.05	9.47	1.56
	3.92	1.18	0.18	3.11	1.18	0.23			
0.10	23.98	7.22	1.1	23.98	9.26	1.57	24.52	9.08	1.52
	3.81	1.15	0.17	3.2	1.31	0.26			
0.11	22.69	6.83	1.04	22.78	8.92	1.53	23.14	8.72	1.47
	3.75	1.13	0.17	3.12	1.31	0.27			
0.12	21.54	6.48	0.99	21.64	8.67	1.51	21.9	8.37	1.43
	3.78	1.14	0.17	3.15	1.41	0.31			
0.13	20.47	6.16	0.94	20.7	8.42	1.48	20.78	8.05	1.39
	3.75	1.13	0.17	3.08	1.44	0.33			
0.14	19.27	5.8	0.88	19.53	8.15	1.46	19.77	7.75	1.36
	3.79	1.14	0.17	3.16	1.59	0.37			

Table 3.28. Simulation Results
Number of treatments = 3
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -3.5$ (median initial mortality),
$\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01

γ_1	Poisson			ZIP			True values		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.22	13.91	2.11	46.14	14.43	2.21	46.05	13.86	2.11
	3.63	1.09	0.17	3.3	1.08	0.16			
0.01	45.85	13.8	2.1	45.97	14.39	2.2	45.71	13.78	2.09
	3.6	1.08	0.16	3.31	1.08	0.17			
0.02	45.15	13.59	2.07	45.6	14.31	2.19	45.21	13.68	2.08
	3.57	1.07	0.16	3.31	1.09	0.17			
0.03	44.01	13.25	2.01	44.89	14.16	2.17	44.48	13.57	2.07
	3.63	1.09	0.17	3.36	1.13	0.17			
0.04	42.47	12.78	1.94	44	13.98	2.14	43.47	13.45	2.06
	3.79	1.14	0.17	3.49	1.21	0.18			
0.05	40.59	12.22	1.86	43	13.82	2.12	42.2	13.32	2.04
	4.03	1.21	0.18	3.53	1.33	0.2			
0.06	38.3	11.53	1.75	41.83	13.65	2.09	40.69	13.17	2.03
	4.29	1.29	0.2	3.75	1.52	0.23			
0.07	35.86	10.8	1.64	40.71	13.54	2.08	39.03	13.01	2.02
	4.5	1.35	0.21	4.04	1.75	0.26			
0.08	32.95	9.92	1.51	39.33	13.38	2.06	37.29	12.84	2.01
	4.63	1.39	0.21	4.44	2.06	0.31			
0.09	30.17	9.08	1.38	37.97	13.22	2.04	35.56	12.66	1.99
	4.4	1.32	0.2	4.87	2.49	0.37			
0.10	27.76	8.36	1.27	36.68	13.02	2.01	33.88	12.46	1.98
	4.25	1.28	0.19	5.37	2.86	0.43			
0.11	26.5	7.98	1.21	36.2	13	2.01	32.27	12.26	1.97
	3.99	1.2	0.18	5.43	3.08	0.46			
0.12	25.47	7.67	1.17	35.7	12.95	2	30.77	12.05	1.95
	3.63	1.09	0.17	5.63	3.33	0.5			
0.13	25.16	7.57	1.15	36.05	13.21	2.04	29.36	11.83	1.94
	3.4	1.02	0.16	5.33	3.43	0.52			
0.14	24.78	7.46	1.13	35.31	12.95	2	28.05	11.61	1.93
	3.29	0.99	0.15	5.51	3.5	0.53			

Table 3.29. Simulation Results
Number of treatments = 4
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -3.5$ (median initial mortality),
$\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01

γ_1	Poisson			ZIP			True values		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.39	13.97	2.12	46.51	14.47	2.21	46.05	13.86	2.11
	3.01	0.9	0.14	2.96	0.92	0.14			
0.01	46.02	13.85	2.11	46.21	14.42	2.2	45.71	13.78	2.09
	3.01	0.91	0.14	2.95	0.92	0.14			
0.02	45.4	13.67	2.08	45.73	14.33	2.19	45.21	13.68	2.08
	3.03	0.91	0.14	2.97	0.93	0.14			
0.03	44.36	13.35	2.03	44.96	14.17	2.17	44.48	13.57	2.07
	3.04	0.91	0.14	3	0.95	0.14			
0.04	42.87	12.9	1.96	43.9	13.96	2.14	43.47	13.45	2.06
	3.08	0.93	0.14	3.17	0.98	0.15			
0.05	41.05	12.36	1.88	42.37	13.73	2.11	42.2	13.32	2.04
	3.13	0.94	0.14	3.27	1.04	0.16			
0.06	39.21	11.8	1.79	40.65	13.51	2.09	40.69	13.17	2.03
	3.29	0.99	0.15	3.43	1.13	0.17			
0.07	37.35	11.24	1.71	38.69	13.34	2.07	39.03	13.01	2.02
	3.39	1.02	0.16	3.33	1.21	0.19			
0.08	35.59	10.71	1.63	36.82	13.23	2.05	37.29	12.84	2.01
	3.63	1.09	0.17	3.18	1.35	0.2			
0.09	33.69	10.14	1.54	35.08	13.11	2.04	35.56	12.66	1.99
	3.73	1.12	0.17	2.82	1.51	0.22			
0.10	31.92	9.61	1.46	33.71	13.09	2.03	33.88	12.46	1.98
	3.95	1.19	0.18	2.71	1.72	0.25			
0.11	30.02	9.04	1.37	32.49	13.07	2.03	32.27	12.26	1.97
	4.07	1.22	0.19	2.52	1.89	0.27			
0.12	28.01	8.43	1.28	31.37	12.99	2.02	30.77	12.05	1.95
	4.09	1.23	0.19	2.51	2.12	0.31			
0.13	26.07	7.85	1.19	30.37	12.79	1.99	29.36	11.83	1.94
	4.06	1.22	0.19	2.58	2.29	0.33			
0.14	24.13	7.26	1.1	29.22	12.7	1.99	28.05	11.61	1.93
	3.78	1.14	0.17	2.93	2.69	0.39			

Table 3.30. Simulation Results
Number of treatment = 5,
True values: β_0 = 3.5, β_1 = -0.05, γ_0 = -3.5 (median initial mortality)
γ_1 = (0.00 to 0.10) by 0.01

γ_1	Poisson			ZIP			True values		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.48	13.99	2.13	46.63	14.5	2.22	46.05	13.86	2.11
	2.66	0.8	0.12	2.53	0.79	0.12			
0.01	46.09	13.87	2.11	46.28	14.44	2.21	45.71	13.78	2.09
	2.73	0.82	0.12	2.54	0.8	0.12			
0.02	45.5	13.7	2.08	45.82	14.35	2.19	45.21	13.68	2.08
	2.73	0.82	0.12	2.53	0.81	0.12			
0.03	44.48	13.39	2.04	45	14.2	2.17	44.48	13.57	2.07
	2.76	0.83	0.13	2.56	0.82	0.13			
0.04	42.97	12.93	1.97	43.8	13.99	2.15	43.47	13.45	2.06
	2.73	0.82	0.12	2.63	0.86	0.13			
0.05	41.25	12.42	1.89	42.39	13.76	2.12	42.2	13.32	2.04
	2.76	0.83	0.13	2.69	0.91	0.14			
0.06	39.38	11.86	1.8	40.92	13.55	2.09	40.69	13.17	2.03
	2.78	0.84	0.13	2.79	0.97	0.15			
0.07	37.51	11.29	1.72	39.13	13.33	2.07	39.03	13.01	2.02
	2.85	0.86	0.13	2.88	1.04	0.16			
0.08	35.78	10.77	1.64	37.41	13.12	2.05	37.29	12.84	2.01
	2.99	0.9	0.14	3.14	1.11	0.17			
0.09	34.1	10.26	1.56	35.51	12.95	2.03	35.56	12.66	1.99
	3.16	0.95	0.14	3.36	1.22	0.19			
0.10	32.54	9.79	1.49	33.53	12.8	2.02	33.88	12.46	1.98
	3.17	0.95	0.14	3.41	1.32	0.21			
0.11	31.22	9.4	1.43	31.78	12.73	2.02	32.27	12.26	1.97
	3.34	1.01	0.15	3.52	1.49	0.23			
0.12	29.77	8.96	1.36	30.08	12.66	2.01	30.77	12.05	1.95
	3.39	1.02	0.15	3.31	1.63	0.24			
0.13	28.6	8.61	1.31	28.94	12.63	2.01	29.36	11.83	1.94
	3.58	1.08	0.16	3.18	1.77	0.26			
0.14	27.11	8.16	1.24	27.45	12.71	2.02	28.05	11.61	1.93
	3.7	1.11	0.17	2.87	2.02	0.3			

Table 3.31. Simulation Results
Number of treatment = 7,
True values: β_0 = 3.5, β_1 = -0.05, γ_0 = -3.5 (median initial mortality)
γ_1 = (0.00 to 0.10) by 0.01

γ_1	Poisson			ZIP			True values		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.35	13.95	2.12	46.54	14.48	2.21	46.05	13.86	2.11
	2.43	0.73	0.11	2.31	0.72	0.11			
0.01	45.97	13.84	2.1	46.19	14.41	2.2	45.71	13.78	2.09
	2.44	0.73	0.11	2.3	0.72	0.11			
0.02	45.36	13.65	2.08	45.69	14.32	2.19	45.21	13.68	2.08
	2.45	0.74	0.11	2.29	0.72	0.11			
0.03	44.31	13.34	2.03	44.86	14.16	2.17	44.48	13.57	2.07
	2.44	0.73	0.11	2.27	0.74	0.11			
0.04	42.78	12.88	1.96	43.66	13.95	2.14	43.47	13.45	2.06
	2.39	0.72	0.11	2.26	0.77	0.12			
0.05	40.97	12.33	1.87	42.2	13.71	2.11	42.2	13.32	2.04
	2.37	0.71	0.11	2.28	0.8	0.12			
0.06	39	11.74	1.78	40.52	13.45	2.08	40.69	13.17	2.03
	2.34	0.7	0.11	2.32	0.85	0.13			
0.07	37.12	11.18	1.7	38.81	13.22	2.05	39.03	13.01	2.02
	2.38	0.72	0.11	2.33	0.9	0.14			
0.08	35.38	10.65	1.62	37.1	13.01	2.03	37.29	12.84	2.01
	2.43	0.73	0.11	2.35	0.97	0.15			
0.09	33.68	10.14	1.54	35.36	12.82	2.01	35.56	12.66	1.99
	2.38	0.72	0.11	2.29	1.04	0.16			
0.10	32.09	9.66	1.47	33.66	12.6	2	33.88	12.46	1.98
	2.33	0.7	0.11	2.25	1.09	0.17			
0.11	30.71	9.24	1.41	32.13	12.42	1.98	32.27	12.26	1.97
	2.42	0.73	0.11	2.38	1.16	0.19			
0.12	29.41	8.85	1.35	30.64	12.21	1.97	30.77	12.05	1.95
	2.52	0.76	0.12	2.56	1.23	0.2			
0.13	28.22	8.5	1.29	29.21	12.03	1.96	29.36	11.83	1.94
	2.65	0.8	0.12	2.79	1.3	0.22			
0.14	27	8.13	1.24	27.74	11.81	1.95	28.05	11.61	1.93
	2.55	0.77	0.12	2.77	1.35	0.23			

Table 3.32. Simulation Results
Number of treatments = 3
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -10.5$ (low initial mortality),
$\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01

γ_1	Poisson			ZIP			True values		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	45.18	13.6	2.07	46.82	14.55	2.22	46.05	13.86	2.11
	3.22	0.97	0.15	3.26	1.11	0.17			
0.01	45.18	13.6	2.07	46.82	14.55	2.22	46.05	13.86	2.11
	3.22	0.97	0.15	3.26	1.11	0.17			
0.02	45.18	13.6	2.07	46.82	14.55	2.22	46.05	13.86	2.11
	3.22	0.97	0.15	3.26	1.11	0.17			
0.03	45.18	13.6	2.07	46.82	14.55	2.22	46.05	13.86	2.11
	3.22	0.97	0.15	3.26	1.11	0.17			
0.04	45.18	13.6	2.07	46.82	14.55	2.22	46.05	13.86	2.11
	3.22	0.97	0.15	3.26	1.11	0.17			
0.05	45.17	13.6	2.07	46.81	14.55	2.22	46.05	13.86	2.11
	3.22	0.97	0.15	3.26	1.11	0.17			
0.06	45.15	13.59	2.07	46.8	14.55	2.22	46.04	13.86	2.11
	3.2	0.96	0.15	3.24	1.1	0.17			
0.07	45.09	13.57	2.06	46.76	14.54	2.22	46.04	13.86	2.11
	3.2	0.96	0.15	3.24	1.1	0.17			
0.08	44.93	13.53	2.06	46.65	14.51	2.21	46.03	13.86	2.11
	3.18	0.96	0.15	3.23	1.11	0.17			
0.09	44.68	13.45	2.04	46.48	14.46	2.21	46.02	13.86	2.11
	3.17	0.95	0.14	3.22	1.12	0.17			
0.10	44.22	13.31	2.02	46.2	14.38	2.19	46	13.86	2.11
	3.06	0.92	0.14	3.15	1.12	0.17			
0.11	43.58	13.12	1.99	45.87	14.26	2.17	45.97	13.86	2.11
	2.99	0.9	0.14	3.07	1.13	0.17			
0.12	43.04	12.96	1.97	45.64	14.17	2.16	45.92	13.86	2.11
	2.9	0.87	0.13	2.99	1.14	0.17			
0.13	42.85	12.9	1.96	45.64	14.17	2.16	45.84	13.86	2.11
	2.86	0.86	0.13	2.95	1.17	0.18			
0.14	42.6	12.82	1.95	45.55	14.14	2.15	45.72	13.86	2.11
	2.88	0.87	0.13	2.91	1.16	0.18			

Table 3.33. Simulation Results
Number of treatments = 4
True values: β_0 = 3.5, β_1 = -0.05, γ_0 = -10.5 (low initial mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson			ZIP			True values		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.2	13.91	2.11	47.51	14.65	2.23	46.05	13.86	2.11
	2.71	0.82	0.12	2.85	0.91	0.14			
0.01	46.2	13.91	2.11	47.51	14.65	2.23	46.05	13.86	2.11
	2.71	0.82	0.12	2.85	0.91	0.14			
0.02	46.2	13.91	2.11	47.51	14.65	2.23	46.05	13.86	2.11
	2.71	0.82	0.12	2.85	0.91	0.14			
0.03	46.2	13.91	2.11	47.51	14.65	2.23	46.05	13.86	2.11
	2.71	0.82	0.12	2.85	0.91	0.14			
0.04	46.2	13.91	2.11	47.5	14.65	2.23	46.05	13.86	2.11
	2.71	0.82	0.12	2.84	0.91	0.14			
0.05	46.19	13.9	2.11	47.5	14.65	2.23	46.05	13.86	2.11
	2.71	0.82	0.12	2.84	0.91	0.14			
0.06	46.18	13.9	2.11	47.49	14.65	2.23	46.04	13.86	2.11
	2.71	0.82	0.12	2.84	0.91	0.14			
0.07	46.14	13.89	2.11	47.48	14.64	2.23	46.04	13.86	2.11
	2.71	0.81	0.12	2.85	0.91	0.14			
0.08	46.04	13.86	2.11	47.43	14.63	2.23	46.03	13.86	2.11
	2.69	0.81	0.12	2.85	0.91	0.14			
0.09	45.85	13.8	2.1	47.36	14.59	2.22	46.02	13.86	2.11
	2.67	0.8	0.12	2.86	0.91	0.14			
0.10	45.46	13.68	2.08	47.25	14.53	2.21	46	13.86	2.11
	2.63	0.79	0.12	2.89	0.91	0.14			
0.11	44.95	13.53	2.06	47.2	14.46	2.2	45.97	13.86	2.11
	2.57	0.77	0.12	2.97	0.92	0.14			
0.12	44.42	13.37	2.03	47.16	14.38	2.19	45.92	13.86	2.11
	2.55	0.77	0.12	3.07	0.93	0.14			
0.13	43.95	13.23	2.01	47.21	14.34	2.18	45.84	13.86	2.11
	2.47	0.74	0.11	3.09	0.92	0.14			
0.14	43.28	13.03	1.98	46.97	14.25	2.17	45.72	13.86	2.11
	2.52	0.76	0.12	3.23	0.97	0.15			

Table 3.34. Simulation Results
Number of treatments = 5
True values: $\beta_0 = 3.5$, $\beta_1 = -0.05$, $\gamma_0 = -10.5$ (low initial mortality),
$\gamma_1 = (0.00 \text{ to } 0.14)$ by 0.01

γ_1	Poisson			ZIP			True values		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.31	13.94	2.12	47.67	14.67	2.24	46.05	13.86	2.11
	2.27	0.68	0.1	2.4	0.77	0.12			
0.01	46.31	13.94	2.12	47.67	14.67	2.24	46.05	13.86	2.11
	2.27	0.68	0.1	2.4	0.77	0.12			
0.02	46.31	13.94	2.12	47.67	14.67	2.24	46.05	13.86	2.11
	2.27	0.68	0.1	2.4	0.77	0.12			
0.03	46.31	13.94	2.12	47.67	14.67	2.24	46.05	13.86	2.11
	2.27	0.68	0.1	2.4	0.77	0.12			
0.04	46.31	13.94	2.12	47.67	14.67	2.24	46.05	13.86	2.11
	2.27	0.68	0.1	2.4	0.77	0.12			
0.05	46.31	13.94	2.12	47.66	14.67	2.23	46.05	13.86	2.11
	2.27	0.68	0.1	2.4	0.77	0.12			
0.06	46.29	13.93	2.12	47.65	14.67	2.23	46.04	13.86	2.11
	2.27	0.68	0.1	2.41	0.78	0.12			
0.07	46.25	13.92	2.12	47.64	14.66	2.23	46.04	13.86	2.11
	2.27	0.68	0.1	2.41	0.78	0.12			
0.08	46.18	13.9	2.11	47.61	14.65	2.23	46.03	13.86	2.11
	2.27	0.68	0.1	2.42	0.78	0.12			
0.09	45.98	13.84	2.1	47.53	14.62	2.23	46.02	13.86	2.11
	2.26	0.68	0.1	2.43	0.78	0.12			
0.10	45.64	13.74	2.09	47.39	14.57	2.22	46	13.86	2.11
	2.26	0.68	0.1	2.45	0.79	0.12			
0.11	45.14	13.59	2.07	47.23	14.5	2.21	45.97	13.86	2.11
	2.2	0.66	0.1	2.49	0.8	0.12			
0.12	44.59	13.42	2.04	47.01	14.42	2.19	45.92	13.86	2.11
	2.16	0.65	0.1	2.52	0.8	0.12			
0.13	43.97	13.24	2.01	46.77	14.36	2.18	45.84	13.86	2.11
	2.12	0.64	0.1	2.54	0.82	0.13			
0.14	43.24	13.02	1.98	46.42	14.27	2.17	45.72	13.86	2.11
	2.09	0.63	0.10	2.62	0.85	0.13			

Table 3.35. Simulation Results
Number of treatments = 7
True values: β_0 = 3.5, β_1 = -0.05, γ_0 = -10.5 (low initial mortality),
γ_1 = (0.00 to 0.14) by 0.01

γ_1	Poisson			ZIP			True values		
	IC90	IC50	IC10	IC90	IC50	IC10	IC90	IC50	IC10
0.00	46.23	13.92	2.12	47.57	14.64	2.23	46.05	13.86	2.11
	2.11	0.64	0.1	2.21	0.7	0.11			
0.01	46.24	13.92	2.12	47.58	14.64	2.23	46.05	13.86	2.11
	2.1	0.63	0.1	2.18	0.69	0.11			
0.02	46.23	13.92	2.12	47.57	14.64	2.23	46.05	13.86	2.11
	2.11	0.64	0.1	2.21	0.7	0.11			
0.03	46.23	13.92	2.12	47.56	14.64	2.23	46.05	13.86	2.11
	2.11	0.64	0.1	2.21	0.7	0.11			
0.04	46.22	13.92	2.12	47.56	14.64	2.23	46.05	13.86	2.11
	2.11	0.64	0.1	2.21	0.7	0.11			
0.05	46.23	13.92	2.12	47.56	14.64	2.23	46.05	13.86	2.11
	2.11	0.64	0.1	2.21	0.7	0.11			
0.06	46.22	13.91	2.11	47.57	14.64	2.23	46.04	13.86	2.11
	2.09	0.63	0.1	2.17	0.69	0.11			
0.07	46.19	13.9	2.11	47.55	14.64	2.23	46.04	13.86	2.11
	2.09	0.63	0.1	2.17	0.69	0.11			
0.08	46.11	13.88	2.11	47.52	14.62	2.23	46.03	13.86	2.11
	2.08	0.63	0.1	2.17	0.69	0.11			
0.09	45.93	13.83	2.1	47.43	14.59	2.22	46.02	13.86	2.11
	2.08	0.62	0.09	2.18	0.69	0.11			
0.10	45.61	13.73	2.09	47.29	14.54	2.21	46	13.86	2.11
	2.07	0.62	0.09	2.23	0.71	0.11			
0.11	45.11	13.58	2.06	47.08	14.47	2.2	45.97	13.86	2.11
	2.04	0.61	0.09	2.24	0.72	0.11			
0.12	44.48	13.39	2.04	46.85	14.38	2.19	45.92	13.86	2.11
	2.01	0.61	0.09	2.27	0.73	0.11			
0.13	43.83	13.2	2.01	46.62	14.31	2.18	45.84	13.86	2.11
	1.92	0.58	0.09	2.26	0.72	0.11			
0.14	43.03	12.95	1.97	46.21	14.2	2.16	45.72	13.86	2.11
	1.94	0.58	0.09	2.38	0.76	0.12			

3.9 Results of Simulation Study

In the low mortality category ($\gamma_0 = -10.5$), the Poisson model has a higher log likelihood for $\gamma_1 < 0.14$ than the ZIP model., however the differences are relatively small (Figure 3.5). In this category, the mortality probability is almost zero, hence one should expect the ZIP model to be not as good as the Poisson model.

Figure 3.5. Difference in the log(likelihood) of ZIP and Poisson model at low mortality (PDF, 4K, Fig3-5.pdf).

In the medium mortality category ($\gamma_0 = -3.5$), the difference in the log likelihood is larger for higher values of γ_1 (Figure 3.6). The higher the treatment level the simulation has, the bigger the difference in the log likelihood between the two models. This makes sense because the mortality probability at the higher γ_1 is almost the same as in the high mortality group. However, this is not true for lower values of γ_1 ($\gamma_1 < 0.03$). In this range, the 3 treatment level simulation produced a larger difference in the log likelihood than the 4, 5, 7 treatment level groups (Figure 3.6).

Figure 3.6. Difference in the log(likelihood) of ZIP and Poisson model at medium mortality (PDF, 4K, Fig3-6.pdf)

In the high natural mortality category ($\gamma_0 = -1.5$), the Poisson model underestimates the intercept terms in the range of 3.22 - 3.3 (true value = 3.5). From Figure 3.7, it can be seen that the ZIP model is better than the Poisson model based on the difference in the log likelihood, especially at higher treatment levels (7 treatments) simulation. For the higher treatment level simulation (4, 5, 7), the difference of the log likelihood peaked at a range of $0.05 < \gamma_1 < 0.08$ at then went back down at higher range of γ_1 ($\gamma_1 > 0.08$). However, for the 3 treatment levels simulation, the difference of log likelihood reached a local maximum at $\gamma_1 = 0.07$, and then went down and up before it peaked at $\gamma_1 = 0.15$. At this value ($\gamma_1 = 0.15$), the ZIP model has some convergence problem because of the high mortality probability. The ZIP model seems to have the best performance among all the runs at 7 treatment levels and $\gamma_1 = 0.09$, because the log likelihood difference (108.23) is the largest.

Figure 3.7. Difference in the log(likelihood) of ZIP and Poisson model at high mortality (PDF, 4K, Fig3-7.pdf)

The estimates of the IC levels for the Poisson model are in general more conservative than the ZIP models. The ZIP models give relatively higher IC levels than the Poisson model in all cases except at the low range of γ_1 ($\gamma_1 < 0.02$) in the high mortality category (please refer to Table 3.17-Table 3.28 for the comparison of IC_{10}, IC_{50}, and IC_{90}, and please refer to Figure 3.8-10 for only IC_{50} with only 3 treatment levels). In the low initial mortality ($\gamma_0 = -10.5$) category, the Poisson model's IC estimates is closer to the true value at the low range of γ_1 ($0 < \gamma_1 < 0.08$) than at the high range $0.08 < \gamma_1 < 0.14$. In medium mortality category, the ZIP model does much better than the Poisson model for $\gamma_1 > 0.02$. The IC_{50} estimation of the Poisson model sharply moved below the true IC_{50} value in this range.

Figure 3.8. IC_{50} of the ZIP and Poisson model at low mortality(PDF, 3K, Fig3-8.pdf)

Figure 3.9. IC_{50} of the ZIP and Poisson model at medium mortality(PDF, 4K, Fig3-9.pdf)

Figure 3.10. IC_{50} of the ZIP and Poisson model at high mortality(PDF, 4K, Fig3-10.pdf)

In general, the Poisson part of the ZIP model does relatively well in estimating the regression coefficients in all cases. On the other hand, the logistic part of the ZIP models does not perform as well as the Poisson part of the model, but it does improve slightly as the number of treatment levels and sample size increases. Due to the high zero proportion in certain runs of the simulation, the logistic part of the ZIP model does have some problems in converging or getting a significant result and this highly affects the performance of the logistic part of the ZIP model.

Based on the results of the simulation study, one should use the regular Poisson model at very low mortality where mortality probability is below 0.3 (i.e. about 3 out of 10 subject died per treatment). On the other hand, one should use the ZIP model at high and medium mortality categories where the mortality probabilities is in the range of 0.3 to 0.8. Even though the simulation study does not cover where the mortality probability is over 0.8, I would suggest one uses the mixture model with caution. It is because the logistic part of the mixture model may not converge due to the high mortality. Improving the experimental designs of the toxicity tests may solve the convergence problem. This can be done by placing more design points within the range of the toxicant concentrations that produce mortality probabilities around 0.9. However, as mentioned in the previous section, if the information about mortality is ignored in the experiment, there may be a problem in knowing how many subject died during the experiment. Since the underlying assumption of the model states that the extra zeroes are due to mortality, one can always apply some preliminary test on the sample distribution of the data to see if the Poisson assumption holds.

3.10 Conclusion

The traditional potency estimation method for chronic bioassays do not take into account mortality which may occur during the experiment. Standard estimation may be inappropriate and highly biased if many deaths occur during the experiment. The mixture model presented here is able to incorporate the extra zeroes due to mortality. Likelihood ratio tests indicate that the mixture model does describe the data better than the regular Poisson model in several example data sets. A simulation study was carried out to compare the ZIP model and Poisson model. The study not only looks at a comparison of the two models, but also looks at how different mortality rates affect the performances of the two models. The differences in the log likelihood of the two models were calculated together with the IC levels. The difference in the log likelihood between the ZIP and Poisson model increases as the number of treatments increases; this is because the total number of observations also increases as the number of treatment increases. The ZIP model has a higher log-likelihood than the regular Poisson model in all cases except in the low mortality category at the range of γ_1, $0 < \gamma_1 < 0.11$. However, the differences in the log likelihood in the low mortality category are very small. The estimation of the regression coefficients of both the Poisson part of the ZIP model and the regular Poisson model are very close to the true values in the low mortality category. In other cases, the ZIP model is better than the Poisson model. In general, the ZIP models have a better overall performance than the regular Poisson models. Especially in medium and high mortality category, the ZIP model really outperformed the Poisson model.

In this chapter, the same covariates are used in both the Poisson part and the logistic part of the ZIP models. Since reproduction and mortality may be affected differently by different toxicants, it seems sensible to use different covariates in the two different parts of the ZIP models. In addition to comparing the different models based on the likelihood, this chapter also considers the calculation of the IC levels and their confidence intervals for only the simplest single regressor model. This can be extended to the more complicated models involving more than one toxicant and even interactions, but the calculation and interpretation will be more difficult. Also, this chapter discusses a mixture model using zeroes and discrete (Poisson) distribution. It can be extended to other studies which involve continuous data. By using different distributional assumptions, it can be applied in a number of situations.