On the Specification of Likelihood Functions for Matched Case-Control Designs: Implications for Resource Selection Studies

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Authorization to Submit Dissertation

This thesis of Elizabeth L. Ng, submitted for the degree of Master of Science with a Major in Statistical Science and titled "On the Specification of Likelihood Functions for Matched Case-Control Designs: Implications for Resource Selection Studies," has been reviewed in final form. Permission, as indicated by the signatures and dates below, is now granted to submit final copies to the College of Graduate Studies for approval.

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Abstract

Matched case-control designs are used in ecology and wildlife management to estimate resource selection functions, which provide insight into habitat use by animals. Recent suggestions to incorporate random effects into these models have little statistical justification because they incorrectly assume unconstrained sampling of study sites, ignoring matching in the study design. Matched case-control designs have been used extensively in epidemiology, where conditional likelihood functions are used to account for constrained sampling. Here, we illustrate the discrepancies between the constrained and unconstrained models, and evaluate the bias of parameter estimates using simulation. We evaluated the conditional logistic model, which produces consistent estimates, and compared results with estimates from prospective logistic models, stratified case-control models, and marginal logistic models. Conditional logistic models had the lowest bias across a wide range of sampling schemes and parameter values. In contrast, marginal logistic models tended to have greater bias and poor confidence interval coverage rates.

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Dedication

This thesis is dedicated to my loving and supportive family:
Ed, Marla, and Ellen.

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CHAPTER 1

Introduction

OVERVIEW

Understanding how animals select habitat and resources is of fundamental importance in ecological studies and natural resource management. Resource selection plays a critical role in population regulation, coexistence, and evolution (Morris, 2003). On a practical level, resource and habitat selection are vital considerations when developing management strategies for threatened and endangered species (Chetkiewicz and Boyce, 2009; Johnson et al., 2004). The importance of estimating and predicting resource selection has given rise to resource selection functions (RSF), a class of models that produce estimates that are proportional to the probability of resource use (Boyce et al., 2002; McLoughlin et al., 2010). Combined with information about available habitat characteristics, RSF models can provide predictions of habitat use across a wide variety of scales (Boyce, 2006; Johnson, 1980).

Many of the approaches for statistical modeling of RSFs have origins in epidemiology (Keating and Cherry, 2004). Instead of modeling habitat use or nonuse, epidemiologists model the probability of disease incidence and the effects of various exposure variables (Breslow and Day, 1980; Collett, 2003). A thorough understanding of the history and development of these models provides context and guidance for appropriate methods of data analysis. In particular, unbiased inference depends on using the correct likelihood function, based on the probability model specified for the data, including the sampling design. However, recent suggestions to use mixed-effects logistic regression to estimate RSF models fail to account for the sampling design (Gillies et al., 2006). Ignoring the sampling design results in an incorrect likelihood function that produces biased parameter estimates.

In the following introduction, we discuss the estimation of RSFs and present pertinent epidemiological literature. We describe models developed for prospective and retrospective sampling designs, including the conditional logistic model for matched

case-control data. In Chapter 2, we present the derivation of the likelihood for data collected using a matched case-control design (i.e., the conditional logistic model), and highlight discrepancies between it and the suggested mixed-effects likelihood function. In Chapter 3, we use simulations to evaluate the bias of estimates from the mixed-effects model relative to the conditional model. Finally, in Chapter 4, we discuss the implications of estimating parameters of retrospective RSF models using models for prospective designs.

PROSPECTIVE AND CROSS-SECTIONAL DESIGNS

When habitat use is common and animals are easily observed, researchers can make inference about the probability of resource use from a random sample of locations across a landscape (Keating and Cherry, 2004). This design is analogous to a prospective or cross-sectional study in epidemiology, where a random sample is taken from the population of interest and patients are followed or observed to see if the disease develops (Collett, 2003). In the random sampling RSF design, a sample (e.g., simple random sample or stratified by covariates) of sites is observed. A binary response variable y is defined such that $y_i = 1$ if the site is used and $y_i = 0$ if it is unused, where i indicates the observation from the i-th site. In addition, p covariates are measured at each site $\mathbf{x}_i' = (x_{i1}, \ldots, x_{ip})$. Then the probability of use conditional on the observed site characteristics is modeled: $P(y_i|\mathbf{x}_i, \alpha, \boldsymbol{\beta})$, where α is the intercept parameter and $\boldsymbol{\beta}' = (\beta_1, \ldots, \beta_p)$ is the vector of covariate coefficients. A logistic model for the probability of use can be assumed

$$P(y_i = 1|\mathbf{x}_i, \alpha, \boldsymbol{\beta}) = \frac{\exp(\alpha + \boldsymbol{\beta}'\mathbf{x}_i)}{1 + \exp(\alpha + \boldsymbol{\beta}'\mathbf{x}_i)}. \tag{1.1}$$

The joint likelihood is the product over all n sites

$$\mathcal{L}(\alpha, \boldsymbol{\beta}) = \prod_{i=1}^{n} \frac{\exp(\alpha + \boldsymbol{\beta}'\mathbf{x}_i)}{1 + \exp(\alpha + \boldsymbol{\beta}'\mathbf{x}_i)}. \tag{1.2}$$

Parameters of the logistic model can be estimated using maximum likelihood (Hosmer et al., 2013). Since all the parameters are identifiable, the probability of site use given the habitat characteristics (i.e., $P[y_i = 1|\mathbf{x}_i, \alpha, \boldsymbol{\beta}]$) can be estimated or predicted given habitat covaraite values at a new site(Keating and Cherry, 2004).

RETROSPECTIVE DESIGNS

When habitat use is rare, a random sample of sites from the landscape may not yield a sufficient number of used sites for analysis (Keating and Cherry, 2004). This is analogous to the study of rare diseases in epidemiology, where a random sample from the population may not capture any individuals who develop the disease (Breslow, 1996; Mann, 2003). Therefore, sampling is conducted retrospectively, once disease status is already known. In these situations, a retrospective case-control design may be used (Breslow, 1996; Thomas and Taylor, 2006). In contrast to the random sampling approach, sampling in case-control studies is stratified by the *outcome* variable y, and a random sample is taken from each stratum (i.e., cases $y = 1$ and controls $y = 0$). As a consequence, the number of used sites (cases) and unused sites (controls) are fixed by design. Covariates ($\mathbf{x}$) are also measured. The retrospective sampling approach effectively reverses the prospective model; y is now the independent variable instead of $\mathbf{x}$. Since sampling is conducted conditional on the outcome variable, the form of the likelihood function is based on $P(\mathbf{x}_i|y_i = 1)$, which reverses the conditioning from Equation 1.1. An assumption of this model is that sampling is conducted independently of the covariates. That is, if t is an indicator variable for inclusion of the observation in the sample, then given y, $\mathbf{x}$ and t are independent.

The retrospective design requires two main changes in inference from the prospective design. First, the probability of use in the sample no longer reflects the probability of use in the population because it depends on the sampling rates (Keating and Cherry, 2004). To illustrate this, we let t be an indicator variable for site inclusion in the sample, such that $t = 1$ for observed sites and $t = 0$ for unobserved sties. Then $\tau_1 = P(t = 1|y = 1)$ is the probability of selection for a case, and $\tau_0 = P(t = 1|y = 0)$ is the probability of selection for a control. Assuming a logistic model, the probability

that a site in the sample will be a used site (i.e., a case) is

$$P(y_i = 1|\mathbf{x}_i, \alpha, \boldsymbol{\beta}, t = 1) = \frac{\exp[\ln(\tau_1/\tau_0) + \alpha + \boldsymbol{\beta}'\mathbf{x}_i]}{1 + \exp[\ln(\tau_1/\tau_0) + \alpha + \boldsymbol{\beta}'\mathbf{x}_i]}. \tag{1.3}$$

If τ_1 and τ_0 are unknown, then the probability of habitat use cannot be evaluated because τ_1, τ_0, and α are not individually identifiable; only their sum $[\ln(\tau_1/\tau_0) + \alpha]$ can be estimated. However, the odds ratios can still be estimated because the intercept cancels from the term.

The second consequence is that the case-control likelihood function is in terms of $P(\mathbf{x}|y)$, rather than the desired $P(y|\mathbf{x})$. Although y is treated as the independent variable for sampling convenience, we ultimately wish to make inference about y dependent on $\mathbf{x}$. Using $P(y|\mathbf{x})$ avoids making multivariate distributional assumptions for $\mathbf{x}$ and also allows prediction of y from $\mathbf{x}$. Anderson (1972) used the fact that $P(\mathbf{x}|y) = P(y|\mathbf{x})P(\mathbf{x})/P(y)$ to factor the case-control likelihood function into a contribution from the prospective logistic model (Equation 1.1) and a contribution from the marginal probabilities of the covariates, which results in a likelihood function where the parameters are constrained by the marginal probabilities of the outcome variable (Breslow, 1996). Anderson (1972) used Lagrange multipliers to demonstrate that $\hat{\boldsymbol{\beta}}$ obtained from the constrained maximum likelihood are algebraically equivalent to those using the unconstrained maximization of Equation 1.3. Farewell (1979) and Prentice and Pyke (1979) used slightly different approaches from Anderson, but also illustrated the mathematical equivalence of the unconstrained and constrained estimates. Furthermore, Prentice and Pyke (1979) showed that the unconstrained maximization also yielded consistent estimates of the covariance matrix for $\hat{\boldsymbol{\beta}}$. The derivations of Anderson (1972), Farewell (1979), and Prentice and Pyke (1979) demonstrated that although the number of cases and controls is fixed by design in retrospective sampling, the likelihood function can be maximized without constraints to obtain equivalent maximum likelihood estimates and standard errors.

Using the unconstrained likelihood function for estimation of case-control models is convenient; however, the observations are dependent due to the sampling design. The prospective logistic regression model produces appropriate parameter estimates

and standard errors, but is not the true retrospective likelihood function for case-control data. Farewell (1979) emphasized this point, stating that mathematical equivalency does not imply the independence of the samples from the case-control study, as given by Equation 1.3. As a result, we cannot assume that the prospective likelihood function will provide unbiased parameter estimates and standard errors for more complex study designs or modeling approaches, such as the matched case-control design (Farewell, 1979; Prentice and Pyke, 1979).

MATCHED CASE-CONTROL DESIGNS

Matched case-control studies are an extension of case-control studies, and arise due stratification of cases and controls by another variable or variables (Hosmer et al., 2013). The design within each stratum or level of the matching variable is a case-control study, but the effects of the other covariates are assumed to be identical after accounting for stratification. In epidemiological studies, patients may be matched based on factors such as age, sex, or location, which affect disease incidence but are not the main factors of interest in the study. Matching based on these nuisance variables can reduce confounding with the variables of interest and can increase statistical efficiency (Breslow, 1996; Rose and van der Laan, 2009). In RSF studies, stratification may result from making multiple observations of used sites from an individual animal (e.g., from telemetry), and pairing them with a random sample of nearby unused sites (Johnson et al., 2004; Gillies et al., 2006). When multiple animals are observed in this manner, observations from each animal comprise a stratum (i.e., matched set or cluster of observations). For example, m_i sites may be observed for the i-th animal in a matched case-control RSF study. Of these observations, c_i sites are used and $m_i - c_i$ sites are unused by design. If there are $i = 1, 2, \ldots, n$ animals in the study, then there are n clusters of observations. Although matching by individual animal is the most common type of stratification in RSF studies (Thomas and Taylor, 2006), matching may also arise due to seasonal sampling or measurement by different observers. In addition to providing logistical advantages, matched case-control studies may also provide insight into the process of habitat selection at finer, more

ecologically relevant scales than either case-control or random sampling RSF studies (Boyce, 2006; McLoughlin et al., 2010; Northrup et al., 2013). Therefore, appropriate inference and estimation are important.

Stratification in matched case-control designs can be accommodated by incorporating design variables (i.e., indicator variables; Hosmer et al. 2013) for strata, since ignoring matching may result in biased parameter estimates (Breslow and Day, 1980; Pike et al., 1980; Breslow and Cain, 1988). The model therefore allows the intercept to vary for each matched set

$$P(y_{ij} = 1|\mathbf{x}_{ij}, \alpha_i, \boldsymbol{\beta}) = \frac{\exp(\alpha_i + \boldsymbol{\beta}'\mathbf{x}_{ij})}{1 + \exp(\alpha_i + \boldsymbol{\beta}'\mathbf{x}_{ij})}, \tag{1.4}$$

where α_i is the effect for the i-th cluster and $j = 1, 2, \ldots m_i$ indexes the observations within the i-th cluster. Model parameters are estimated consistently when when the number of observations per cluster is large. However, estimators are not consistent if the number of parameters increases with sample size (Neyman and Scott, 1948; Prentice and Pyke, 1979). The model can be modified in two ways to reduce the number of parameters to estimate.

The first approach is to treat the individual-specific effects (i.e., $\alpha_1, \ldots,$ $alpha_n$) as nuisance parameters and condition on a sufficient statistic for those parameters (i.e., the number of used locations in each cluster; Molenberghs and Verbeke 2006). Conditioning on a sufficient statistic eliminates the nuisance parameters from the likelihood function (Gail et al., 1981; Scott and Wild, 1991), which reduces the number of parameters to estimate, thereby improving the asymptotic behavior of the likelihood function. Additionally, conditioning on the total number of used sites per cluster accounts for the dependency among the observations due to the sampling design (Craiu et al., 2011). Despite the benefits of using a conditional likelihood function, a closed form may not exist for all model parameters. Therefore developing closed-form conditional likelihood functions for other parameters (e.g., slope parameters) is not possible outside of special cases (Diggle et al., 1998).

The second approach for handling individual-specific parameters is to use random effects (Molenberghs and Verbeke, 2006). In the random-effects approach, the cluster-

specific effects are considered random draws from a population of effects, for which a distribution can be assumed. The parameters are then eliminated by marginalization (Molenberghs and Verbeke, 2006). Recently, a random-effects approach has been suggested to estimate the parameters of RSF models for matched case-control designs (Gillies et al., 2006; Nielson et al., 2012), and has been used in a number of applications (e.g., Hebblewhite and Merrill 2008; Chetkiewicz and Boyce 2009; Koper and Manseau 2009). As we illustrate in the next section, there is no theoretical justification to use such a random-effects approach. Intuitively, the random-effects approach is incorrect because it only accounts for one source of dependency present in the data. Specifically, Gillies et al. (2006) state that "using logistic regression... assumes independence among observations", and suggested that generalized linear mixed effects models (GLMM) could account for dependency and pseudoreplication. However, this is precisely the conclusion that Farewell (1979) warns against in his derivation of the use of logistic regression for case-control studies. The proposal to use random effects accounts for the nesting of observations within each animal, but neglects the dependence among observations due to conditional sampling.

In the next section, we illustrate the conditional logistic model for matched case-control data (Breslow and Day, 1980) and contrast it with the GLMM proposed by Gillies et al. (2006). We then evaluate the effects of the misspecified model on parameter estimation using simulation. Finally, we identify sampling and design considerations that are important for study design, and discuss the consequences for natural resource managers.

CHAPTER 2

Models for Matched Case-Control Data

CONDITIONAL LOGISTIC MODELS

A number of derivations for the conditional likelihood model have been presented (Breslow and Day, 1980; Collett, 2003; Hosmer et al., 2013). Here, we review previous work and provide a simple example for illustration. Finally, we contrast the conditional logistic model with the mixed-effects logistic model proposed by Gillies et al. (2006).

Consider a matched case-control study with $i = 1, 2, \ldots, n$ animals. For the i-th animal, $j = 1, 2, \ldots, m_i$ sites are observed, of which c_i used locations and $m_i - c_i$ unused locations are observed. The response, y_{ij}, is equal to one for used sites and equal to zero for unused sites. Thus the total number of sites used by the i-th individual is $c_i = \sum_{j=1}^{m_i} y_{ij}$. Because sampling is conducted conditional on y, m_i and c_i are fixed by design. We also define S_i to be the set of indices of the observations of individual i for which $y_{ij} = 1$, and $\bar{S}_i$ to be the set of indices of the observations of the individual for which $y_{ij} = 0$. Habitat covariates of interest are measured at each site. For simplicity, we assume that a single discrete covariate x_{ij} is measured.

As a simple example, assume we have collected data for a single animal ($n = 1$), and omit the subscript i for simplicity. We observe a total of $m = 4$ observations, where the first two sites are used ($c = 2$) and the second two sites are unused ($m - c = 2$). We also measure a habitat covariate (x) from each site. The data are presented in Table 2.1. Here, $S = \{1, 2\}$ and $\bar{S} = \{3, 4\}$.

Since the observations are made conditional on the status of the sites (i.e., used or unused), we begin with the retrospective likelihood function of the form $P(x_{ij}|y_{ij}, \alpha, \beta)$, where α is the intercept parameter and β is the parameter corresponding to x. For brevity, conditioning on α and β in the following derivation is implied throughout. Under the assumption of independence between observations, the joint likelihood

TABLE 2.1: Example data set of $m = 4$ observations (indexed by j) from a single animal. One covariate x is measured for each observation. The status (response) of each site is given by y, where 1 indicates use and 0 indicates nonuse.

i	j	x	y
1	1	x_1	1
1	2	x_2	1
1	3	x_3	0
1	4	x_4	0

function is given by the product of stratum-specific likelihood functions

$$\prod_{j=1}^{m_i} P(x_{ij}|y_{ij}) = \prod_{j \in S_i} P(x_{ij}|y_{ij} = 1) \times \prod_{j \notin S_i} P(x_{ij}|y_{ij} = 0). \tag{2.1}$$

The conditional likelihood function is given by the probability of the observed data conditional on the probability of c_i used sites out of the total m_i observed sites (i.e., the stratum sums) with the values of x_{ij}. This probability of observing the data is related to the sum of all the possible assignments of the c_i used and $(m_i - c_i)$ unused sites to the m_i observed locations. The number of possible assignments is

$$u_i = \binom{m_i}{c_i} = \frac{m_i!}{c_i!(m_i - c_i)!}.$$

We let $z = 1, 2, \ldots, u_i$ denote the z-th assignment of used and unused statuses among the locations and their habitat values. Then for the z-th assignment of the observed data, S_z is a set of indices of the c_i used locations. This gives the probability of the observed data set, given the values of x_{ij} and the sum c_i

$$\frac{\prod_{j \in S_i} P(x_{ij}|y_{ij} = 1) \times \prod_{j \notin S_i} P(x_{ij}|y_{ij} = 0)}{\sum_{z=1}^{u_i} \left\{ \prod_{j \in S_z} P(x_{ij}|y_{ij} = 1) \times \prod_{j \notin S_z} P(x_{ij}|y_{ij} = 0) \right\}}. \tag{2.2}$$

For our example data set, the numerator of Equation 2.2 is the probability of the observed data, given by

$$\prod_{j \in S} P(x_j|y_j = 1) \times \prod_{j \notin S} (x_j|y_j = 0) = P(x_1|y_1 = 1)P(x_2|y_2 = 1)P(x_3|y_3 = 0)P(x_4|y_4 = 0).$$

For the denominator, there are $u = \binom{4}{2} = 6$ possible ways to permute the indices of the statuses (i.e., used or unused). For this example, we can write out all possible combinations of the c used locations among the observations (Table 2.2).

TABLE 2.2: For $c = 2$ used and $(m - c) = 2$ unused sites, there are $u = 6$ possible assignments of the statuses to the $m = 4$ observations. The permutations are indexed by z, with the observed data set given by $z = 1$. S_z indicates the set of indices of the cases (i.e., used sites).

z	S_z	Cases	Controls
1	{1, 2}	$(x_1, y_1), (x_2, y_2)$	$(x_3, y_3), (x_4, y_4)$
2	{1, 3}	$(x_1, y_1), (x_3, y_3)$	$(x_2, y_2), (x_4, y_4)$
3	{1, 4}	$(x_1, y_1), (x_4, y_4)$	$(x_3, y_3), (x_2, y_2)$
4	{2, 3}	$(x_2, y_2), (x_3, y_3)$	$(x_1, y_1), (x_4, y_4)$
5	{2, 4}	$(x_2, y_2), (x_4, y_4)$	$(x_1, y_1), (x_3, y_3)$
6	{3, 4}	$(x_3, y_3), (x_4, y_4)$	$(x_1, y_1), (x_2, y_2)$

The denominator of Equation 2.2 is the union of the probabilities $P(x_j|y_j)$ for all reorderings of j given by S_z

$$\begin{aligned}
\sum_{z=1}^{6}\left\{\prod_{j\in S_z} P(x_j|y_j=1)\times\prod_{j\notin S_z}(x_j|y_j=0)\right\} = \\
& P(x_1|y_1=1)P(x_2|y_2=1)P(x_3|y_3=0)P(x_4|y_4=0) \\
+\;& P(x_1|y_1=1)P(x_3|y_3=1)P(x_2|y_2=0)P(x_4|y_4=0) \\
+\;& P(x_1|y_1=1)P(x_4|y_4=1)P(x_3|y_3=0)P(x_2|y_2=0) \\
+\;& P(x_2|y_2=1)P(x_3|y_3=1)P(x_1|y_1=0)P(x_4|y_4=0) \\
+\;& P(x_2|y_2=1)P(x_4|y_4=1)P(x_1|y_1=0)P(x_3|y_3=0) \\
+\;& P(x_3|y_3=1)P(x_4|y_4=1)P(x_1|y_1=0)P(x_2|y_2=0).
\end{aligned}$$

Since we aim to make inference about $P(y_{ij}|x_{ij})$, we apply Bayes' theorem to each of the $P(x_{ij}|y_{ij})$ terms, using

$$P(x_{ij}|y_{ij}=1) = \frac{P(y_{ij}=1|x_{ij})P(x_{ij})}{P(y_{ij}=1)}$$

and

$$P(x_{ij}|y_{ij}=0) = \frac{P(y_{ij}=0|x_{ij})P(x_{ij})}{P(y_{ij}=0)},$$

to give

$$\frac{\prod_{j\in S_i}\frac{P(y_{ij}=1|x_{ij})P(x_{ij})}{P(y_{ij}=1)}\times\prod_{j\notin S_i}\frac{P(y_{ij}=0|x_{ij})P(x_{ij})}{P(y_{ij}=0)}}{\sum_{z=1}^{u_i}\left\{\prod_{j\in S_z}\frac{P(y_{ij}=1|x_{ij})P(x_{ij})}{P(y_{ij}=1)}\times\prod_{j\notin S_z}\frac{P(y_{ij}=0|x_{ij})P(x_{ij})}{P(y_{ij}=0)}\right\}}. \tag{2.3}$$

We can factor further

$$\frac{\prod_{j=1}^{m_i}\frac{P(x_{ij})}{P(y_{ij})}\times\prod_{j\in S_i}P(y_{ij}=1|x_{ij})\times\prod_{j\notin S_i}P(y_{ij}=0|x_{ij})}{\prod_{j=1}^{m_i}\frac{P(x_{ij})}{P(y_{ij})}\times\sum_{z=1}^{u_i}\left\{\prod_{j\in S_z}P(y_{ij}=1|x_{ij})\times\prod_{j\notin S_z}P(y_{ij}=0|x_{ij})\right\}} \tag{2.4}$$

and simplify to yield

$$\frac{\prod_{j \in S_i} P(y_{ij} = 1|x_{ij}) \times \prod_{j \notin S_i} P(y_{ij} = 0|x_{ij})}{\sum_{z=1}^{u_i} \left\{ \prod_{j \in S_z} P(y_{ij} = 1|x_{ij}) \times \prod_{j \notin S_z} P(y_{ij} = 0|x_{ij}) \right\}}. \tag{2.5}$$

Note that the likelihood function is now in terms of $P(y_{ij}|x_{ij})$, as in the prospective model.

Let β be the corresponding coefficient of x_{ij}, which we assume is common among the observed individuals. Additionally, let α_i be the individual-specific effect on the probability of habitat use. We assume that the correct logistic model is given by

$$P(y_{ij} = 1|x_{ij}, \alpha_i, \beta) = \frac{e^{\alpha_i + \beta x_{ij}}}{1 + e^{\alpha_i + \beta x_{ij}}}, \tag{2.6}$$

and

$$P(y_{ij} = 0|x_{ij}, \alpha_i, \beta) = \frac{1}{1 + e^{\alpha_i + \beta x_{ij}}}. \tag{2.7}$$

We can substitute Equations 2.6 and 2.7 into the likelihood function (Equation 2.5) and simplify algebraically to obtain

$$\frac{\prod_{j \in S_i} \frac{e^{\alpha_i + \beta x_{ij}}}{1 + e^{\alpha_i + \beta x_{ij}}} \times \prod_{j \notin S_i} \frac{1}{1 + e^{\alpha_i + \beta x_{ij}}}}{\sum_{z=1}^{u_i} \left\{ \prod_{j \in S_z} \frac{e^{\alpha_i + \beta x_{ij}}}{1 + e^{\alpha_i + \beta x_{ij}}} \times \prod_{j \notin S_z} \frac{1}{1 + e^{\alpha_i + \beta x_{ij}}} \right\}}. \tag{2.8}$$

As in Equation 2.4, the $(1 + e^{\alpha_i + \beta x_{ij}})^{-1}$ term will cancel. The α_i term, which is constant for a given individual (i.e., for fixed value of i), will also cancel due to conditioning on the sufficient statistic, $c_i = \sum_{j=1}^{m_i} y_{ij}$. Thus, the joint likelihood function for observations from an individual animal is given by

$$\mathcal{L}_i(\beta) = \frac{\prod_{j \in S_i} e^{\beta x_{ij}}}{\sum_{z=1}^{u_i} \left\{ \prod_{j \in S_z} e^{\beta x_{ij}} \right\}}. \tag{2.9}$$

Finally, we can take the product over all matched sets to obtain the joint likelihood function of all animals, conditional on the number of observed sites for each animal

$$\mathcal{L}(\beta) = \prod_{i=1}^{n} \frac{\prod_{j \in S_i} e^{\beta x_{ij}}}{\sum_{z=1}^{u_i} \left\{ \prod_{j \in S_z} e^{\beta x_{ij}} \right\}}, \tag{2.10}$$

which does not depend on the individual specific effects (α_i). Except in special cases, such as 1:1 matching of cases and controls, Equation 2.10 cannot be maximized using standard logistic regression software (Breslow and Day, 1980; Hosmer et al., 2013). Additionally, maximization can be computationally intensive because the denominator contains a sum with u elements, where u grows as m increases and when c/m is close to 0.5. Numerical methods must therefore be used to maximize Equation 2.10 (Gail et al., 1981; Smith et al., 1981; Scott and Wild, 1991).

MARGINAL LOGISTIC MODELS

If the number of observed sites were not fixed by design, then a prospective or cohort likelihood function could be used, which does not condition on c_i. In contrast to the conditional logistic model, the likelihood function for logistic regression applicable for cohort data is given by

$$\mathcal{L}(\boldsymbol{\alpha}, \beta) = \prod_{i=1}^{n} \prod_{j=1}^{m_i} P(y_{ij} | x_{ij}, \alpha_i, \beta) = \prod_{i=1}^{n} \prod_{j=1}^{m_i} \frac{e^{y_{ij}(\alpha_i + \beta x_{ij})}}{1 + e^{\alpha_i + \beta x_{ij}}}, \tag{2.11}$$

which includes the animal-specific effects, $\boldsymbol{\alpha}' = (\alpha_1, \ldots, \alpha_n)$. If the α_i are treated as fixed effects, this model can be used to estimate parameters of the retrospective model in Equation 1.3, as long as the matching is coarse (i.e., there are few, large clusters), or if the sampling fractions are known (Prentice and Pyke, 1979; Fears and Brown, 1986).

However, Gillies et al. (2006) suggest that the model in Equation 2.11 can be extended to incorporate a random effect for the individuals to allow for heterogeneity in habitat selection and unbalanced designs. Consider the animal-specific effects to

be drawn independently from a distribution, $F(\alpha)$ such as $\alpha_i \sim Normal(0, \sigma_\alpha)$. The distribution function, $F(\alpha)$, may also depend on other parameters (Molenberghs and Verbeke, 2006). We can make inference about β by marginalizing over the distribution of α_i

$$\mathcal{L}_i(\beta, \sigma_\alpha) = \int \prod_{j=1}^{m_i} \frac{e^{y_{ij}(\alpha+\beta x_{ij})}}{1+e^{(\alpha+\beta x_{ij})}} dF(\alpha). \tag{2.12}$$

Specifying the α_i as random effects would solve the problem of an increasing number of parameters with sample size (i.e., number of animals) if the data were collected from a prospective design (Hosmer et al., 2013). For matched case-control data, however, a retrospective likelihood function such as Equation 2.10 is required. Using 2.12 assumes that given α_i, the y_{ij} are independent, which they are not due to the sampling design. Although the work of Anderson (1972), Prentice and Pyke (1979), and Farewell (1979) demonstrated the equivalence of the maximum likelihood estimates and standard errors from fixed effects logistic regression were equivalent to those from the constrained model, there is no justification to extend this approach to the mixed effects case. That is, the equivalence between constrained and unconstrained estimation only holds when the α_i are treated as additional, fixed-effects parameters. The consequences of estimating β using an incorrect likelihood function, however, are unclear and are evaluated using simulation in the next chapter.

CHAPTER 3

Simulations

METHODS

The likelihood function for a matched-case control design is not equivalent to the likelihood function for logistic regression for a prospective design. Consequently, the likelihood function for a mixed-effects logistic regression model is consistent with a prospective or cross-sectional design, but not a retrospective case-control design. Despite the application of mixed-effects logistic regression models for RSFs, little is known about the effects of using these incorrectly specified models for matched case-control data. Furthermore, although the consequences of improperly specifying the model for matched case-control designs can be evaluated for very simple models (e.g., ignoring matching in single binary covariates; Breslow and Day 1980), resource selection models tend to include multiple covariates. We therefore developed a simulation study for matched case-control designs with three continuous covariates of different magnitudes, and a random individual-specific effect. We evaluated a variety of values for the variance of the random effect, as well as the number of individuals (i.e., clusters), the number of cases per cluster (c_i), and the ratio of cases to controls within each cluster. The objectives of the simulation study were to 1) evaluate the behavior of the incorrect mixed-effects logistic regression model in comparison to three other methods, and 2) to evaluate the effects of sampling design on parameter estimates.

Data Generation

A rejection sampler was used to generate data sets that were sampled under a matched case-control design (Appendix A). As in Chapter 2, we considered a design with $i = 1, 2, \ldots, n$ animals, from which $j = 1, 2, \ldots, m_i$ sites are observed. Of the m_i sites, c_i are used (i.e., cases) and $(m_i - c_i)$ are unused (i.e., controls). Since sampling is conducted conditional on the use status, m_i and c_i are known quantities that are fixed

by design, not random variables. The data-generating model was of the form:

$$P(y_{ij} = 1|\mathbf{x}_{ij}, \alpha_i, \boldsymbol{\beta}) = \frac{\exp(\alpha_i + \beta_1 x_{ij1} + \beta_2 x_{ij2} + \beta_3 x_{ij3})}{1 + \exp(\alpha_i + \beta_1 x_{ij1} + \beta_2 x_{ij2} + \beta_3 x_{ij3})}, \tag{3.1}$$

where $P(y_{ij} = 1|\mathbf{x}_{ij}, \alpha_i, \boldsymbol{\beta})$ is the probability that the j-th site from the i-th animal is used, α_i is the individual-specific effect for the i-th animal, and $\mathbf{x}_{ij} = (x_{ij1}, x_{ij2}, x_{ij3})$ are the measured covariates. We assumed that the α_i were independently drawn from a population of individual-specific effects, such that $\alpha_i \sim \text{Normal}(0, \sigma_\alpha)$. Each of the x_{ijk} were independently and identically distributed as $x_{ijk} \sim \text{Uniform}(-2, 2)$. To simulate sampling for the i-th individual under a matched case-control design, we used the following algorithm:

Begin Algorithm

Step 0. Specify σ_α, m_i, c_i, and $\boldsymbol{\beta}$. Set $l_1 = 0$ and $l_0 = 0$

Step 1. Sample α_i from Normal$(0, \sigma_\alpha)$

Step 2. While $l_1 < c_i$

- 2a. Sample each x_{ijk} independently of each other from Uniform$(-2, 2)$
- 2b. Calculate $P(y_{ij} = 1|\mathbf{x}_{ij}, \alpha_i, \boldsymbol{\beta})$ using Equation 3.1
- 2c. Sample y^*_{ij} from Bernoulli$(P[y_{ij} = 1|\mathbf{x}_{ij}, \alpha_i, \boldsymbol{\beta}])$
- 2d. If $y^*_{ij} = 1$, accept $(\mathbf{x}_{ij}, y^*_{ij})$ as an observation and set $l_1 = l_1 + 1$.
- 2e. Return to 2.

Step 3. While $l_0 < (m_i - c_i)$

- 3a. Sample each x_{ijk} independently of each other from Uniform$(-2, 2)$
- 3b. Calculate $P(y_{ij} = 1|\mathbf{x}_{ij}, \alpha_i, \boldsymbol{\beta})$ using Equation 3.1
- 3c. Sample y^*_{ij} from Bernoulli$(P[y_{ij} = 1|\mathbf{x}_{ij}, \alpha_i, \boldsymbol{\beta}])$
- 3d. If $y^*_{ij} = 0$, accept $(\mathbf{x}_{ij}, y^*_{ij})$ as an observation and set $l_0 = l_0 + 1$.
- 3e. Return to 3.

End Algorithm.

The process above was repeated for each of the n individuals, drawing a new α_i for each cluster of observations.

Parameter Estimation

We evaluated parameter estimates using models that assumed four different forms for the likelihood function, each corresponding to a particular model and sampling design. The first model was the conditional logistic model (CLM), which is an appropriate model for the data that avoids estimation of the cluster-specific effects via the conditioning argument in Equation 2.10. The second model was based on Equation 2.12, which was a mixed effects or marginal logistic model (MLM) suggested by Gillies et al. (2006). The third model was a fixed effects logistic regression model for a stratified case control (SCC) design. The SCC leverages the mathematical equivalence of the prospective likelihood and the case-control likelihood for a single strata, and incorporates a fixed effect for each individual (i.e., design variable for cluster). That is, in contrast to the MLM which treats the α_i as random effects, the SCC model treats the α_i as fixed effects. Based on work by Prentice and Pyke (1979) and Fears and Brown (1986), we expect this model to perform well so long as the clusters become large as the number of clusters increases, but the exact sample sizes required are unknown. Finally, the fourth model was a prospective logistic model (PLM), which ignored the matching and sampling constraints of the data. In the PLM, the α_i are assumed to be equivalent for all individuals. Based on work by Breslow and Day (1980) and Pike et al. (1980), ignoring these key factors should lead to biased parameter estimates.

We were primarily interested in comparing estimates from CLM with those from MLM. However, results from SCC and PLM were evaluated to provide further context for the comparison of CLM and MLM. In particular, SCC can be viewed as a special case of MLM where the variance of the random effect is zero. PLM can also be viewed as a special case of SCC, where the individual-specific fixed effects are equal for all animals in the study.

Simulations

Parameter values and sampling designs for the simulations were based on values found in the literature (Thomas et al., 2003; Gillies et al., 2006; Thomas and Taylor, 2006). For simplicity, we assumed that all clusters were of equal size $(m_i = m, \forall i)$

and contained the same number of cases ($c_i = c, \forall i$). We also set $\boldsymbol{\beta}' = (1, 2, 3)$, which allowed us to investigate the effect of parameter magnitude. Values of σ_α used in simulations were 0.1, 1, and 2. We also evaluated the effects of the sampling design by varying the number of used sites per cluster (i.e., cluster size; c), and the ratio of cases to controls ($r = c/m_0$). Values of c were 1, 2, 5, 10, 20, or 80, and values of r were 0.5, 0.2, or 0.1. Finally, combinations of σ_α, c, and r were evaluated for scenarios with $n = 100$ clusters and $n = 30$ clusters. For each combination of parameter values, 150 data sets were randomly generated using the algorithm above.

All models were fit to the simulated data sets using R (R Core Team, 2016), and code is available in Appendix B. We used the `clogit` function in the **survival** package (Therneau and Grambsch, 2000; Therneau, 2015) to fit CLMs, the `glmer` function in the **lme4** package (Bates et al., 2014) to fit MLMs, and the `glm` function to fit SCCs and PLMs. All four models were fit to each simulated data set, and results from models that failed to converge were discarded. Rates of convergence failure were 4.7-5.6% for CLM, 0.6-0.8% for MLM, 3.0-8.0% for SCC, and 0-0.04% for PLM. Estimated parameters and standard errors for $\boldsymbol{\beta}$ were extracted. We calculated $\widehat{\text{Bias}}(\hat{\beta}_p, \beta_p) = \frac{1}{b}\sum_{i=1}^{b}(\hat{\beta}_{p_i} - \beta_{p_i})$, where b is the number of simulations, for $p = 1, 2, 3$. We also determined whether the estimated 95% confidence interval contained the true parameter value for each β_p. Monte Carlo margin of error for $\hat{\beta}_p$ was calculated as $1.96\sqrt{\widehat{\text{Var}}(\hat{\beta}_p)/b}$, where b is the number of simulations that converged for the combination of parameter values. In addition, $\hat{\sigma}_\alpha$ was retained and evaluated for the MLMs.

RESULTS

The results from the simulations were largely consistent with previous research. Results from all four methods are available in Appendix C. For simulations with $n = 100$, results for the estimated bias are provided in Table C.1 and coverage rates are provided in Table C.2. For simulations with $n = 30$, results for the estimated bias are provided in Table C.3 and coverage rates are provided in Table C.4.

Simulation Results for $n = 100$

PLM, which ignored matching in the data by assuming a common intercept, was biased for most values of $\boldsymbol{\beta}$, r, c, and especially for large σ_α (Table C.1). Estimated bias of PLM was negative, except for data sets with $\sigma_\alpha = 0.1$, which were not biased or were slightly positively biased (by up to 4%). The largest magnitude of bias for PLM occurred for β_3 with $\sigma_\alpha = 2$, when $\hat{\beta}_3$ was 25% below the true value. Bias of PLM did not vary with r or c, and was approximately equal to the bias from MLM except when $\sigma_\alpha = 2$. Coverage rates were correlated with the degree of bias; unbiased estimates (when $\sigma_\alpha = 0.1$) had appropriate coverage rates (Table C.2). Since the bias of PLM did not change greatly across the sampling designs evaluated (i.e., values of r and c), results are excluded from the figures below.

SCC treats the α_i as fixed effects, and accounting for clustering in this manner tended to provide improvements over PLM when the individual-specific effects were the greatest (i.e., $\sigma_\alpha = 2$). For example, bias for β_3 was 4% for SCC when $c = 20, r = 0.5$, and $\sigma_\alpha = 2$ (Figure 3.1), compared to -25% for PLM (Table C.1). However, the improvement of SCC over PLM disappeared if c was less than 5, and bias was worse for SCC when $c = 1, 2$. Bias was close to zero for the largest clusters (c = 80), but increased as the number of cases per cluster decreased. As with PLM, bias increased with parameter magnitude. Interestingly, SCC exhibited the largest magnitude of bias out of the four models. In the scenario with 1 case and 2 controls (i.e., $r = 0.5$), $\hat{\beta}_3$ was 85% greater than β_3. Coverage rates were less than the nominal value when bias was greater than about 2% (Figure 3.2).

In contrast to SCC, MLM treats the α_i as random effects. Patterns in bias for MLM were similar to PLM; both produced negatively biased estimates when σ_α was large (Figure 3.1). However, bias of PLM was the same regardless of c and r, whereas the bias of MLM decreased as c increased. When clusters were large, MLM was an improvement over SCC. Estimated bias was essentially zero for MLM with $c = 80$, even for β_3 and with $\sigma_\alpha = 2$, which resulted in 25% bias for PLM. Coverage rates for MLM were better than for PLM or SCC, especially when $\sigma_\alpha = 0.1$, which met nominal rates for all β_p, r, and c (Figure 3.2).

CLM was the least biased of all four methods (Figure 3.1). For most simulations, the bias was well below 5%. Bias was largest for the smallest clusters (i.e., $r = 0.5, c = 1$), where the bias was as large as 26%. However, these cluster sizes also posed estimation challenges for SCC and MLM, which had the highest bias for those values of c and r. Coverage rates were also the most accurate for CLM, even when the parameter estimates were biased. The lowest coverage rate for CLM was 89%, in contrast to the other three models, which had coverage rates as low as 0-21% (Figure 3.2). Although CLM performed well for most values of r, c, $\boldsymbol{\beta}$, and σ_α, it had the highest rates of convergence failure, which prohibited estimation for data sets with $r = 0.5$, $c = 80$, and $\sigma_\alpha = 2$.

Overall, for SCC, MLM, and CLM, the magnitude of the bias was greatest for data sets with the fewest observations per cluster, particularly for SCCs (Figure 3.3). Although bias tended to decrease for MLM and CLM as c increased, the ratio of cases to controls did not have as great an effect as for SCCs (Figure 3.4). With sufficiently large cluster sizes (i.e., large c and low r), both SCC and MLM performed similarly to CLM. Patterns in coverage rates generally mirrored patterns in bias; sampling designs and models that produced the largest magnitude of bias also contained the true parameter value in fewer than 95% of simulations (Figure 3.2). In particular, PLM had the worst coverage rates, which persisted until $c > 20$. MLM performed slightly better than PLM, and required $c > 10$ to attain nominal coverage rates. CLM performed well across all simulations.

For MLM, bias in estimates of $\boldsymbol{\beta}$ for small cluster sizes may be due to underestimation of σ_α (Figure 3.5). Indeed, for the smallest cluster sizes, $\hat{\sigma}_\alpha$ was zero. In these cases, MLM is equivalent to SCC, which treats the σ_α as fixed effects. Although estimates approached the true value as the cluster size increased, the largest clusters evaluated in this study (i.e., $c = 80, m = 800$) did not produce accurate estimates of σ_α (Figure 3.6).

Simulation Results for $n = 30$

Simulation results for $n = 30$ showed similar patterns in bias and converage rates as simulations with $n = 100$, though variation was higher (Figure 3.7, 3.8). The

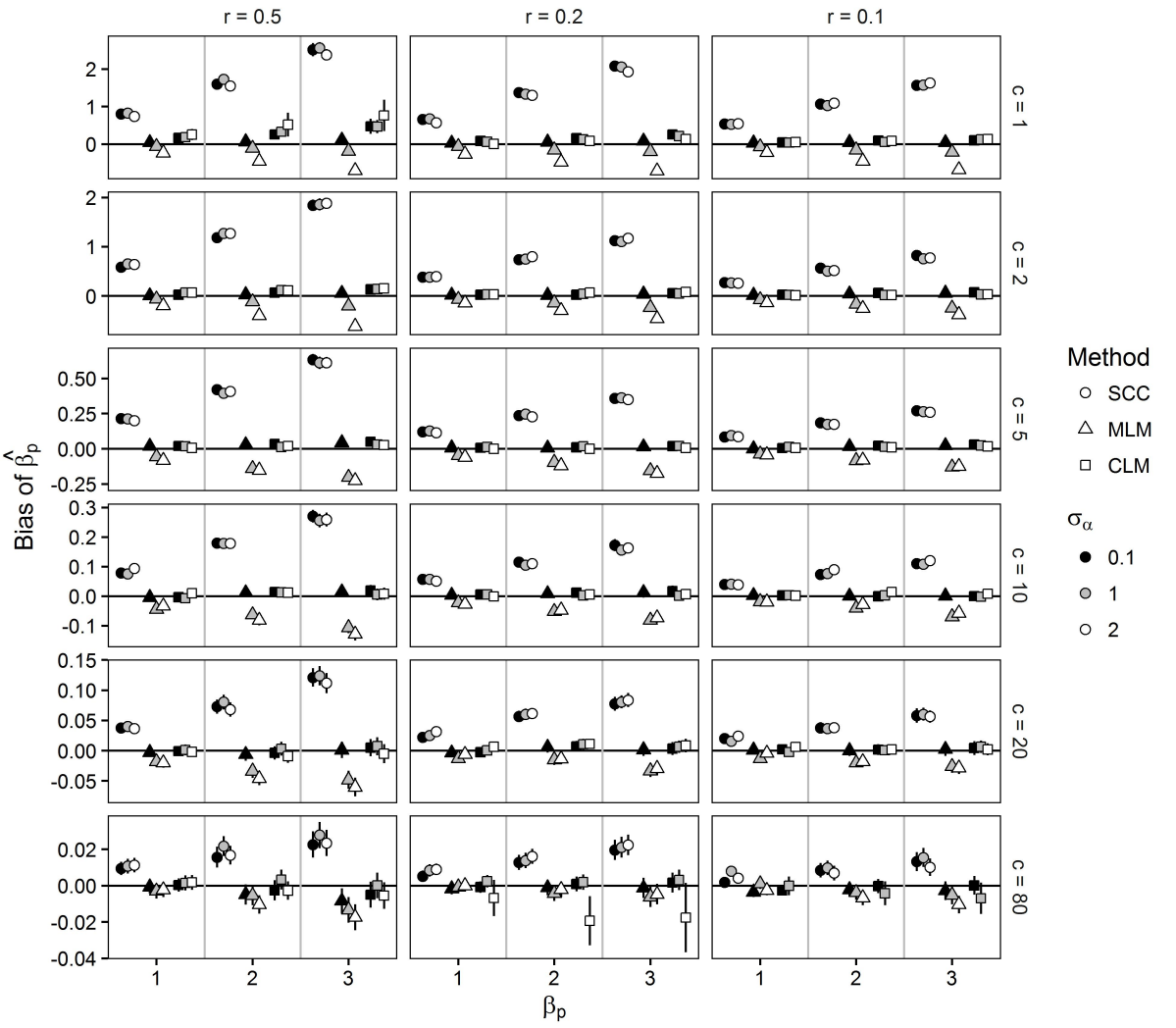

FIGURE 3.1: Bias of $\hat{\boldsymbol{\beta}}$ estimated from a matched case-control design with $n = 100$ using a stratified case-control model (SCC), marginal logistic model (MLM), and conditional logistic model (CLM). The number of cases (c) and ratio of cases to controls (r) varied between simulations. Note the change in scale for bias across different values of c.

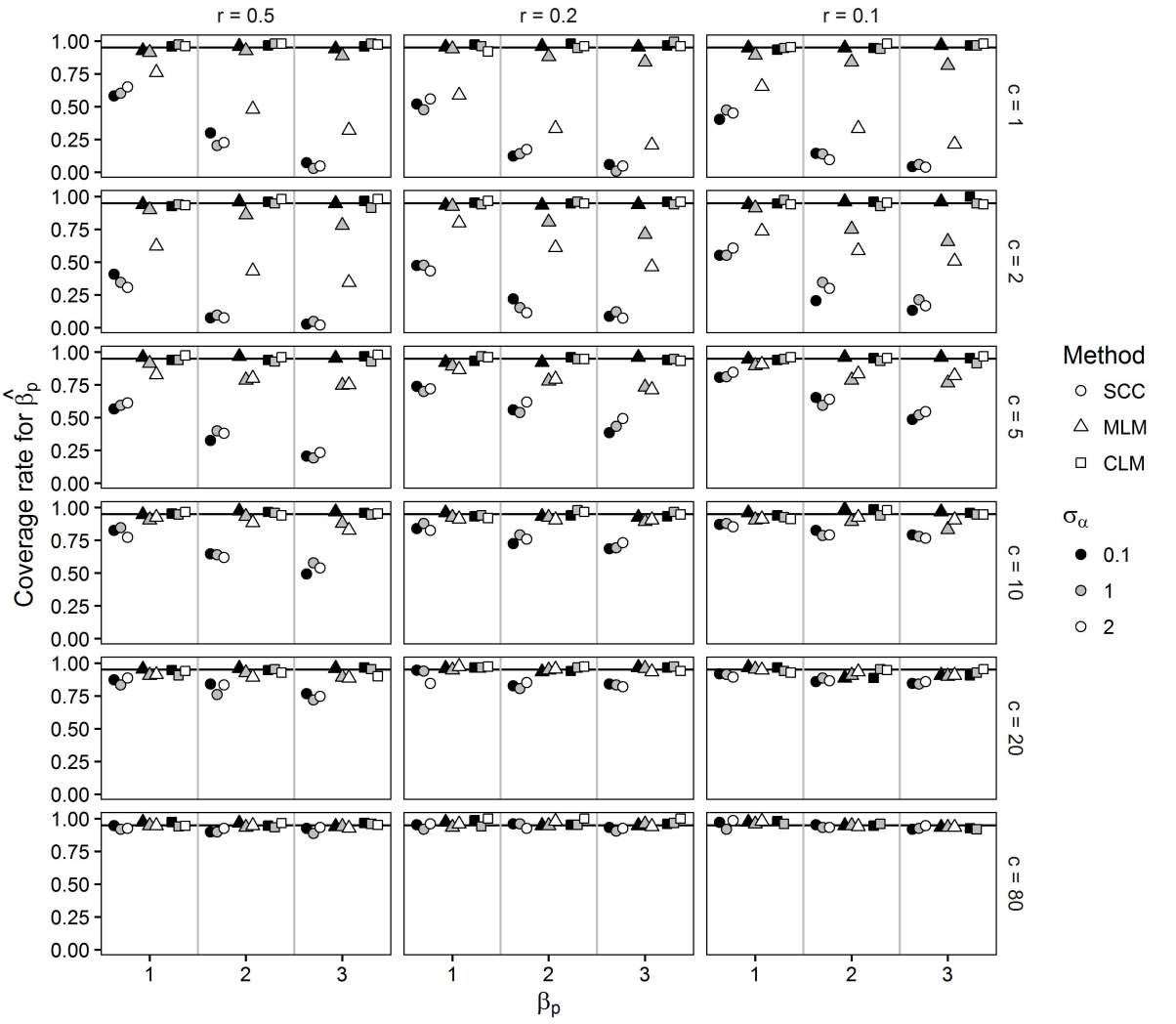

FIGURE 3.2: Realized coverage rates of 95% confidence intervals for $\boldsymbol{\beta}$ estimated from a matched case-control design with $n = 100$ using a stratified case-control model (SCC), marginal logistic model (MLM), and conditional logistic model (CLM). The number of cases (c) and ratio of cases to controls (r) varied between simulations. Horizontal line indicates 95% coverage.

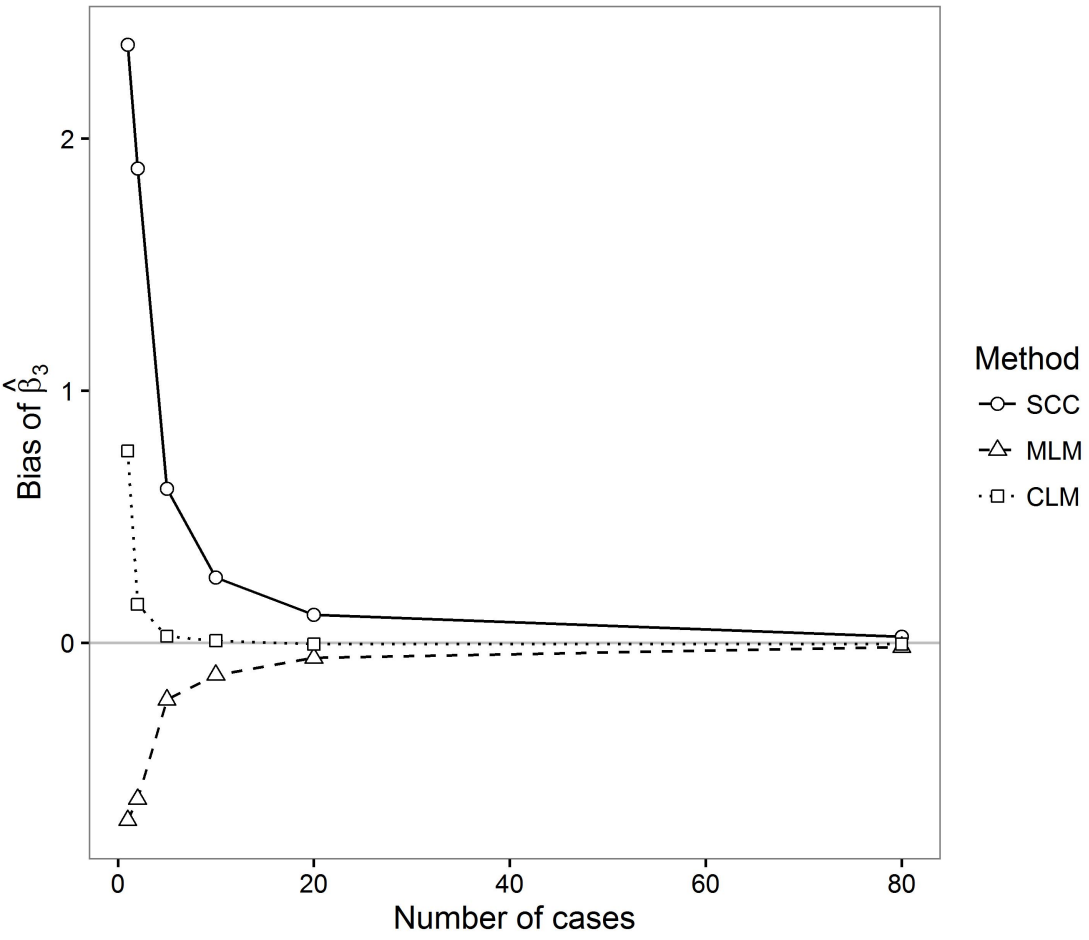

FIGURE 3.3: Bias of $\hat{\beta}_3$ estimated from a matched case-control design with $n = 100$ using a stratified case-control model (SCC), marginal logistic model (MLM), and conditional logistic model (CLM). The number of cases varied but r was fixed at 0.5 and $\sigma_\alpha = 2$.

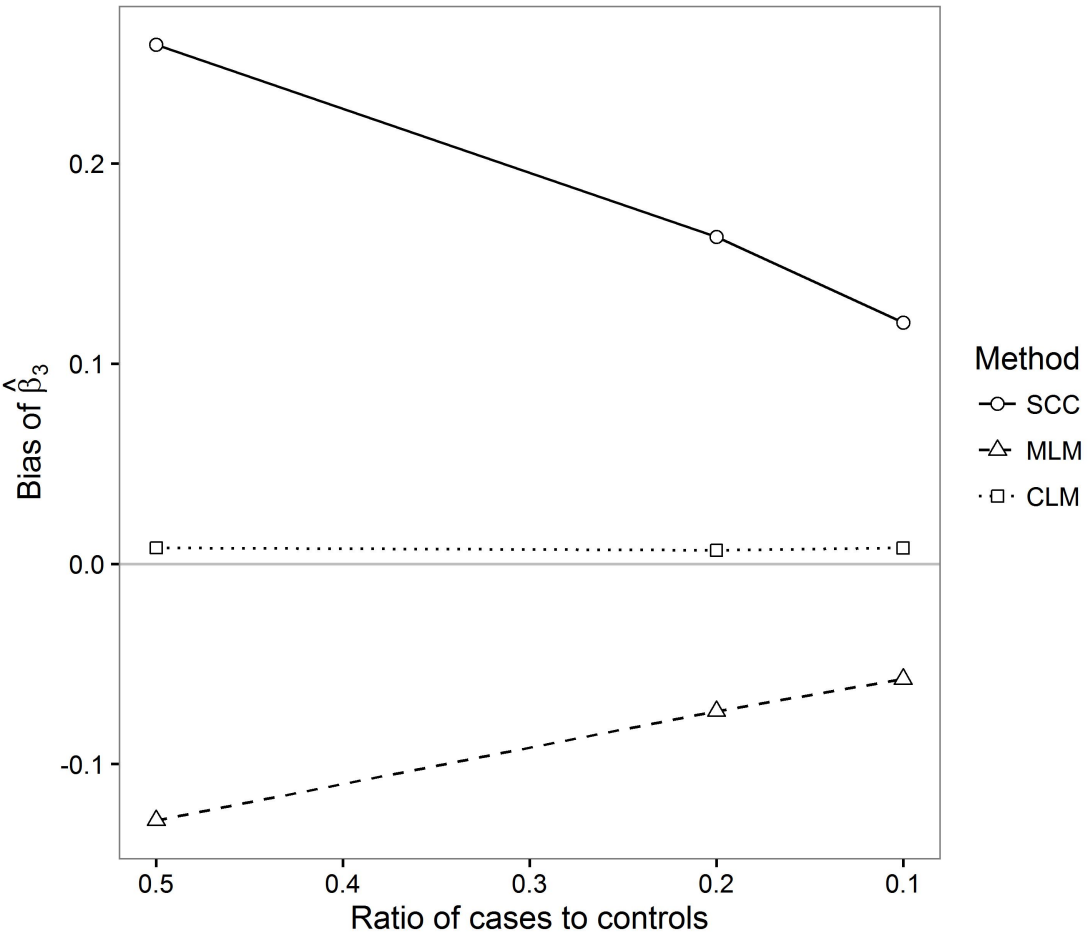

FIGURE 3.4: Bias of $\hat{\beta}_3$ estimated from a matched case-control design with $n = 100$ using a stratified case-control model (SCC), marginal logistic model (MLM), and conditional logistic model (CLM). The ratio of cases to controls varied but c was fixed at 10 and $\sigma_\alpha = 2$.

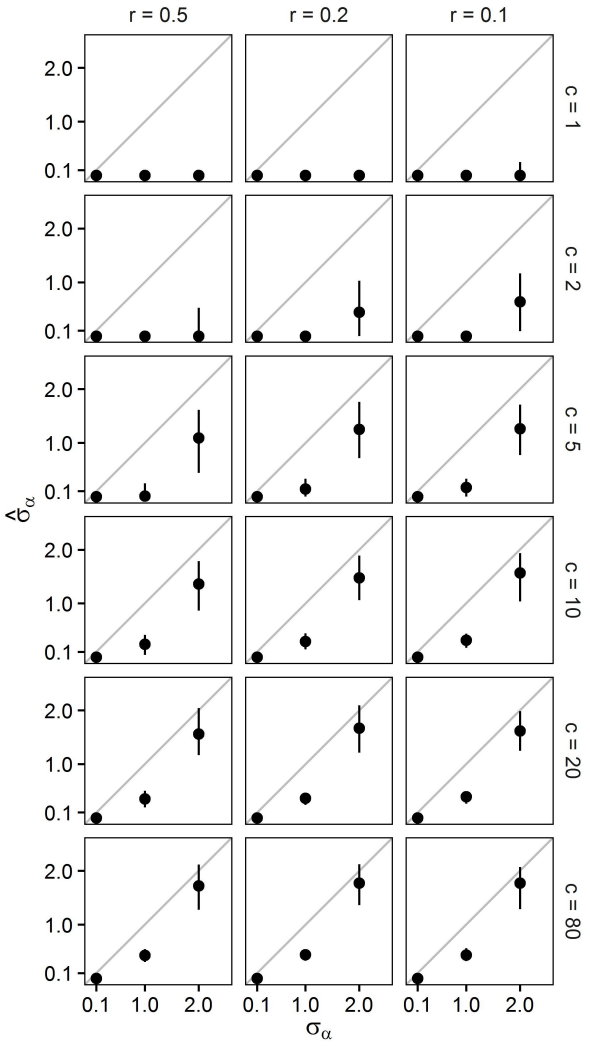

FIGURE 3.5: Estimates of σ_α from a matched case-control design with $n = 100$ fit using a marginal logistic model (MLM) with varying numbers of cases (c) and ratio of cases to controls (r). Unbiased estimates fall on the diagonal (1:1) line.

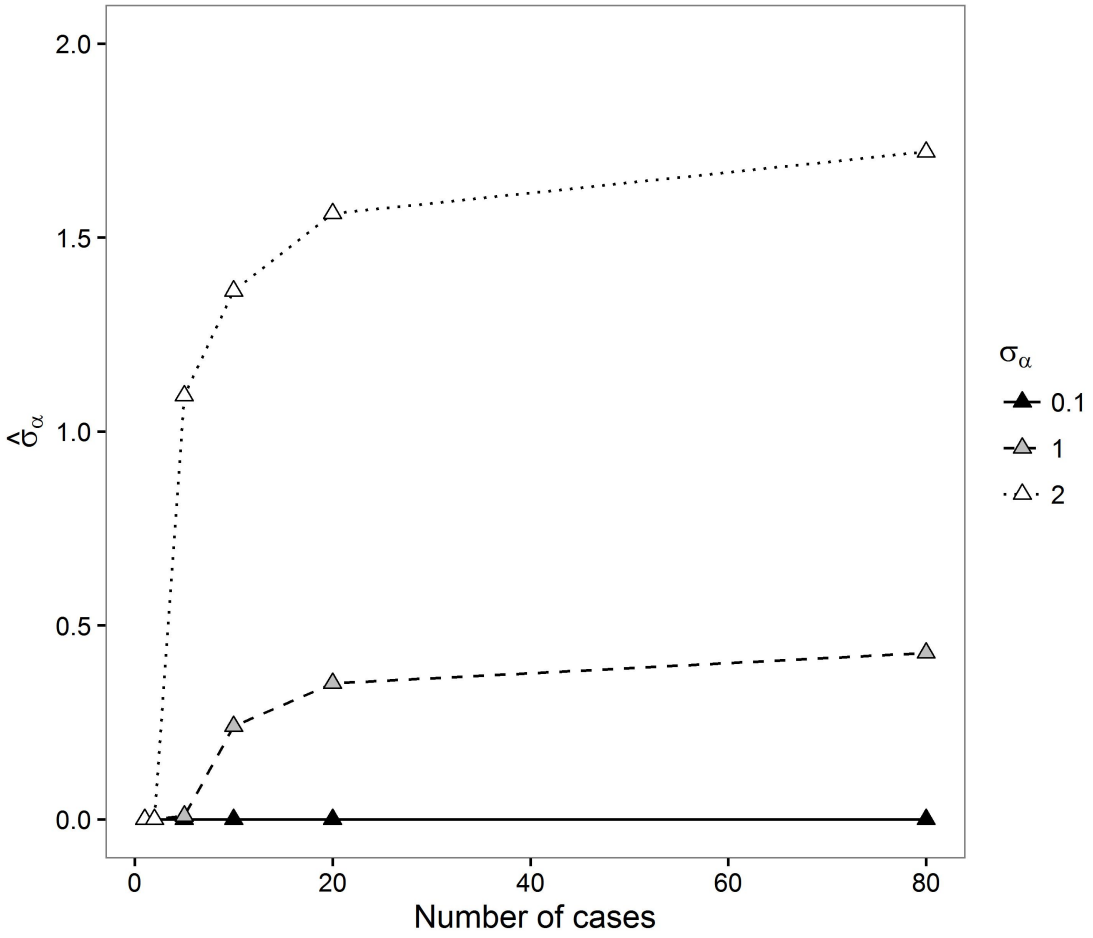

FIGURE 3.6: Estimates of σ_α from a matched case-control design with $n = 100$ fit using a marginal logistic model (MLM) with varying numbers of cases (c) and ratio of cases to controls equal to 0.5.

main differences occurred for very small cluster sizes ($c = 1, r = 0.5$), where all three methods produced positively biased estimates of $\boldsymbol{\beta}$. However, increasing $c > 1$ produced the same patterns as the $n = 100$ simulations (Figure 3.9). Likewise, for some values of c, bias tended to increase slightly as r decreased (Figure 3.10), but most values resembled the results in Figure 3.4. Although the patterns in bias were similar between $n = 100$ and $n = 30$, the magnitude of the bias was higher for small sample sizes for MLM and CLM. For MLM, the maximum percent bias was nearly twice as high with the smaller sample sizes (for β_3 with $c = 1$, $r = 0.$, and $\sigma_\alpha = 2$; Figure 3.7). For CLM, the bias was as high as 140% for β_1 with $c = 1$, $r = 0.5$, and $\sigma_\alpha = 0.1$. However, for CLM, bias greather than 10% of the true value was restricted $c = 1$, and in a few cases, $c = 2$. Estimates from CLM for clusters with more than two observations were nearly unbiased. Maximum bias for PLM and SCC did not change for the larger sample size.

Coverage rates for data sets with $n = 30$ were closer to nominal rates than for $n = 100$ (Figure 3.8). Most methods and sampling designs had appropriate coverage rates for $c > 5$, in contrast to $n = 100$, which required $c > 10$. For CLM, large cluster sizes (i.e., $r = 0.1$ and $c = 80$) once again produced high rates of convergence failure, and models that were estimated tended to produce inaccurate confidence intervals.

Similar to MLM estimates of σ_α with $n = 100$, estimates with $n = 30$ tended to be negatively biased (Figure 3.11). The estimates, particularly for $\sigma_\alpha = 2$, also tended to be much more variable. While increasing the number of cases improved accuracy, σ_α was still underestimated with $c = 80$ (Figure 3.12).

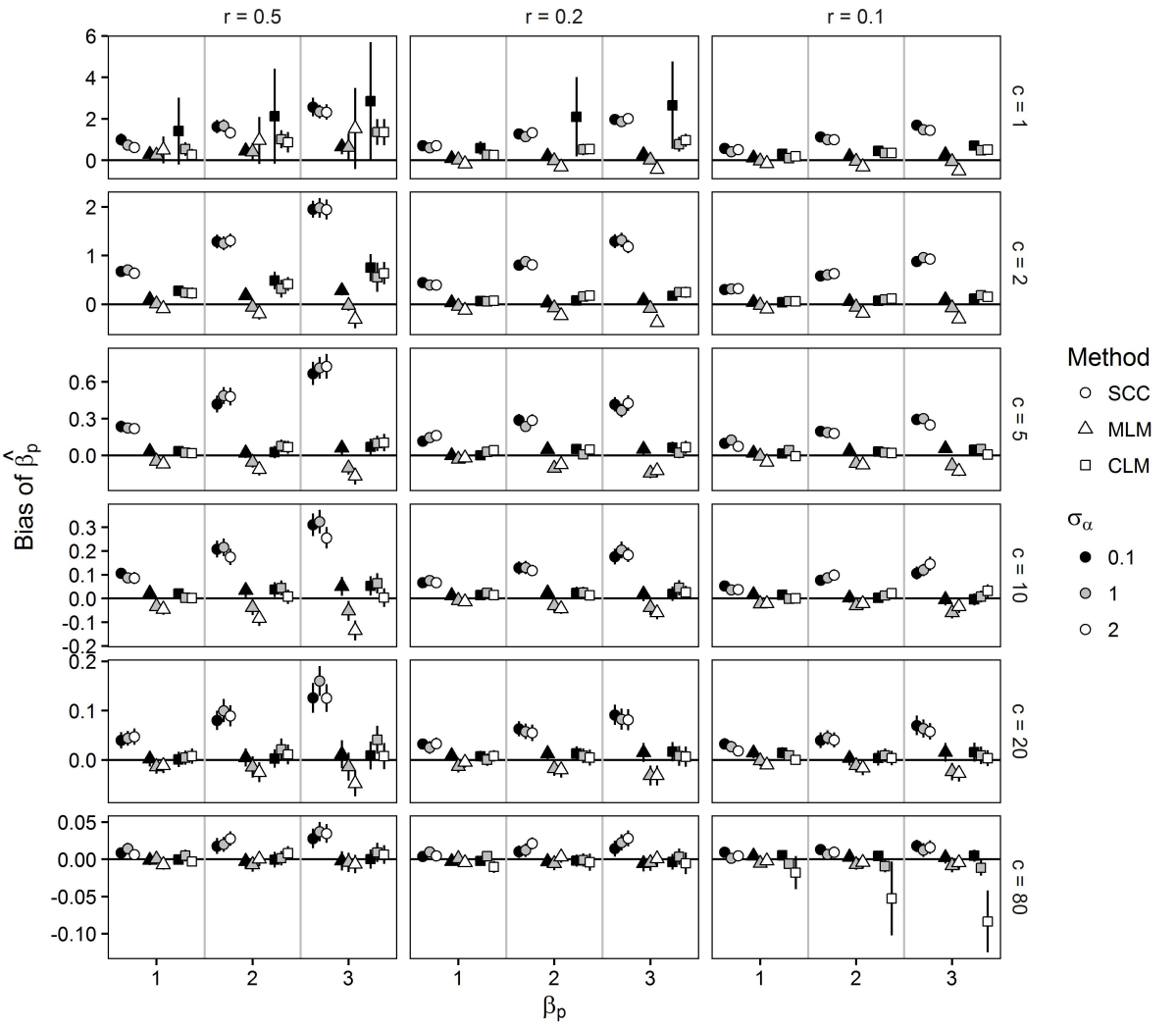

FIGURE 3.7: Bias of $\hat{\boldsymbol{\beta}}$ estimated from a matched case-control design with $n = 30$ using a stratified case-control model (SCC), marginal logistic model (MLM), and conditional logistic model (CLM). The number of cases (c) and ratio of cases to controls (r) varied between simulations. Note the change in scale for bias across different values of c.

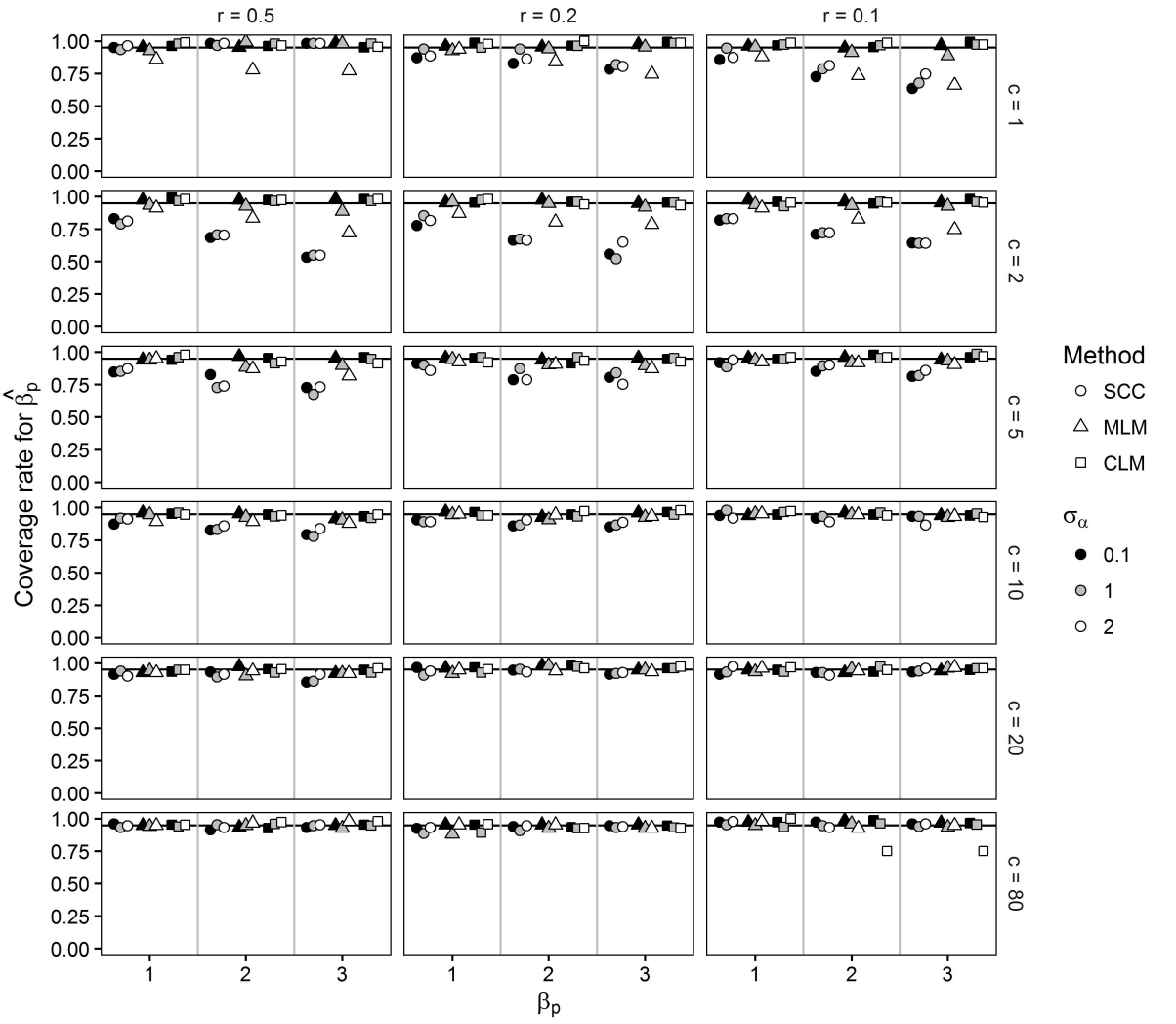

FIGURE 3.8: Realized coverage rates of 95% confidence intervals for $\boldsymbol{\beta}$ estimated from a matched case-control design with $n = 30$ using a stratified case-control model (SCC), marginal logistic model (MLM), and conditional logistic model (CLM). The number of cases (c) and ratio of cases to controls (r) varied between simulations. Horizontal line indicates 95% coverage.

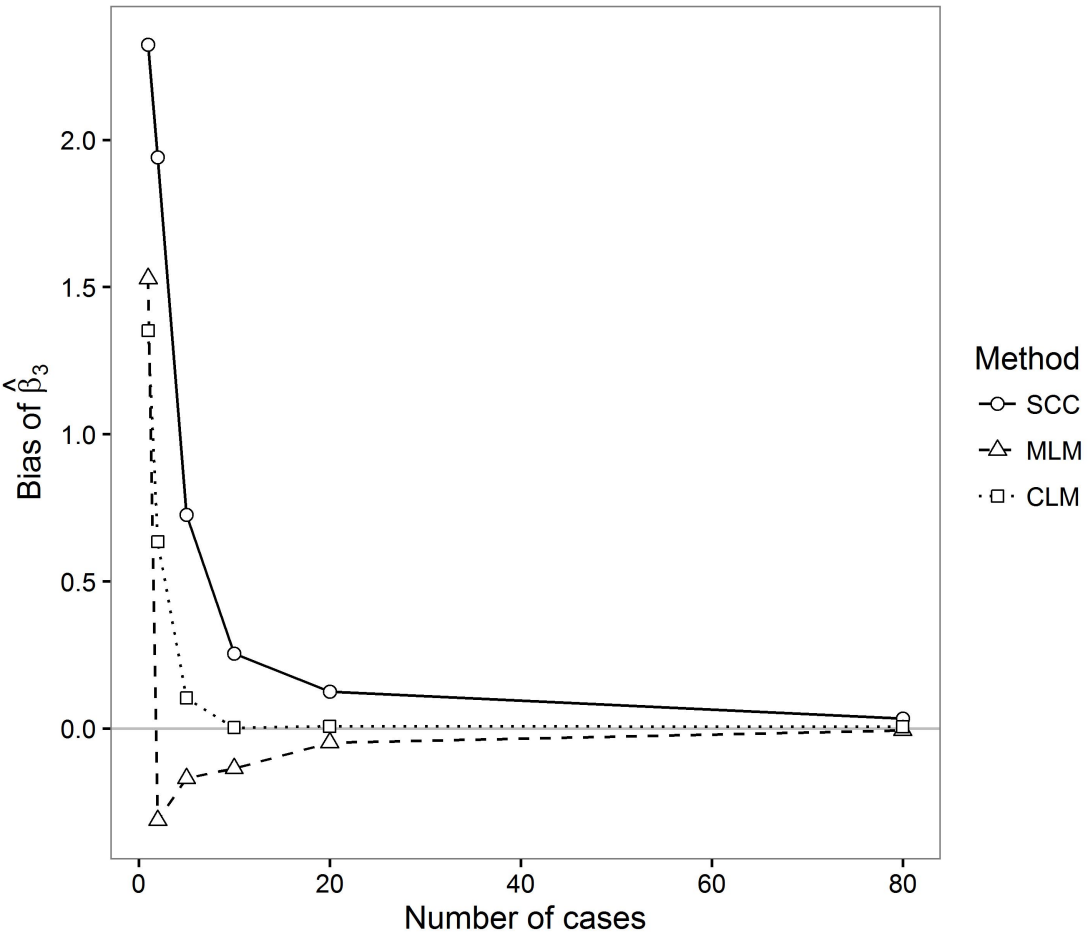

FIGURE 3.9: Bias of $\hat{\beta}_3$ estimated from a matched case-control design with $n = 30$ using a stratified case-control model (SCC), marginal logistic model (MLM), and conditional logistic model (CLM). The number of cases varied but r was fixed at 0.5 and $\sigma_\alpha = 2$.

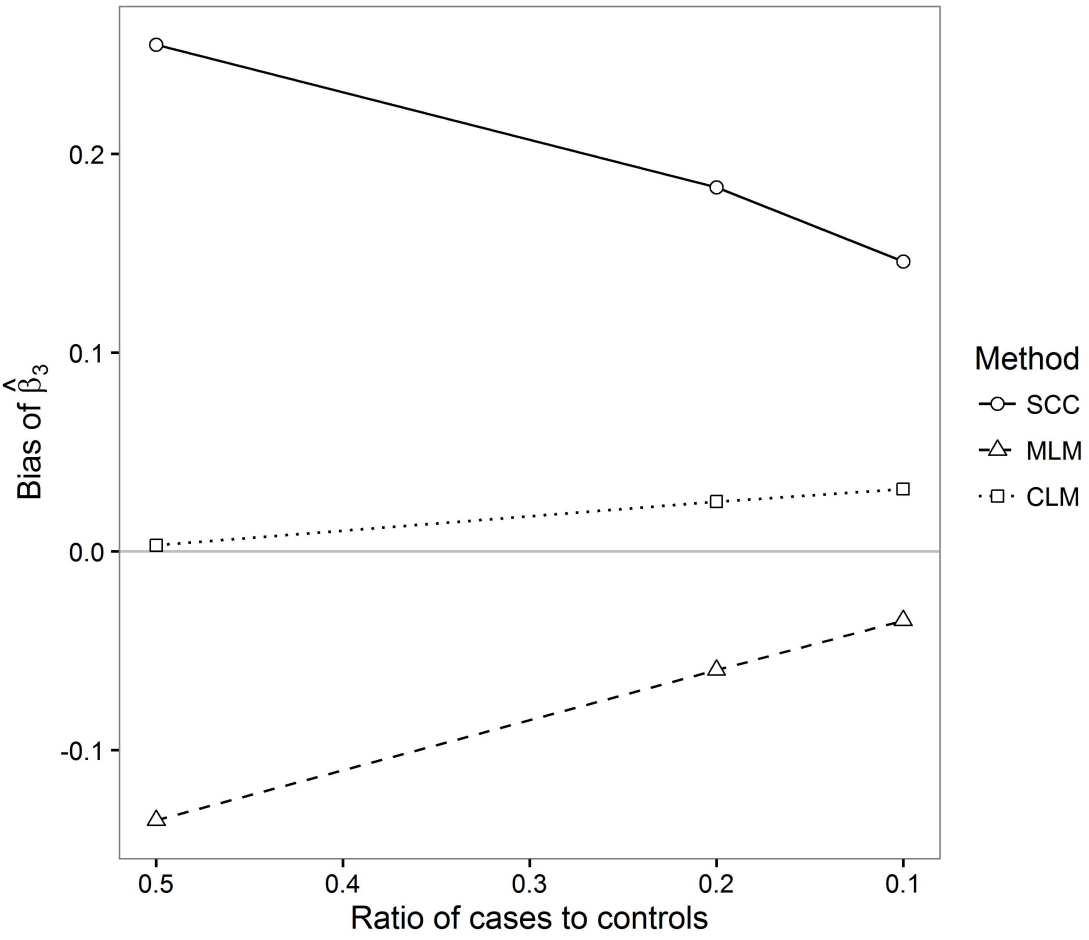

FIGURE 3.10: Bias of $\hat{\beta}_3$ estimated from a matched case-control design with $n = 30$ using a stratified case-control model (SCC), marginal logistic model (MLM), and conditional logistic model (CLM). The ratio of cases to controls varied but c was fixed at 10 and $\sigma_\alpha = 2$.

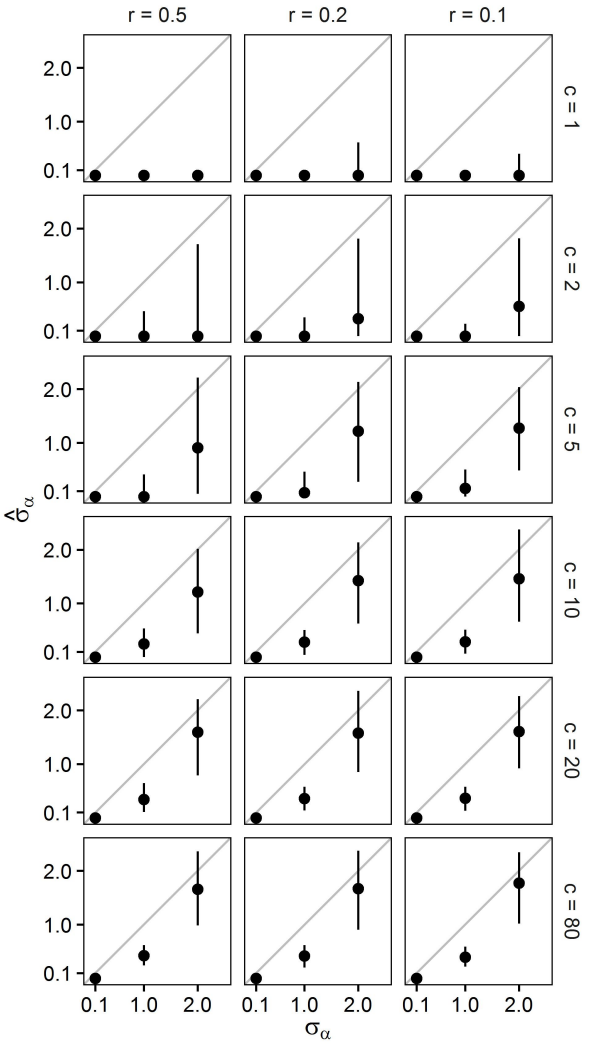

FIGURE 3.11: Estimates of σ_α from a matched case-control design with $n = 30$ fit using a marginal logistic model (MLM) with varying numbers of cases (c) and ratio of cases to controls (r). Unbiased estimates fall on the diagonal (1:1) line.

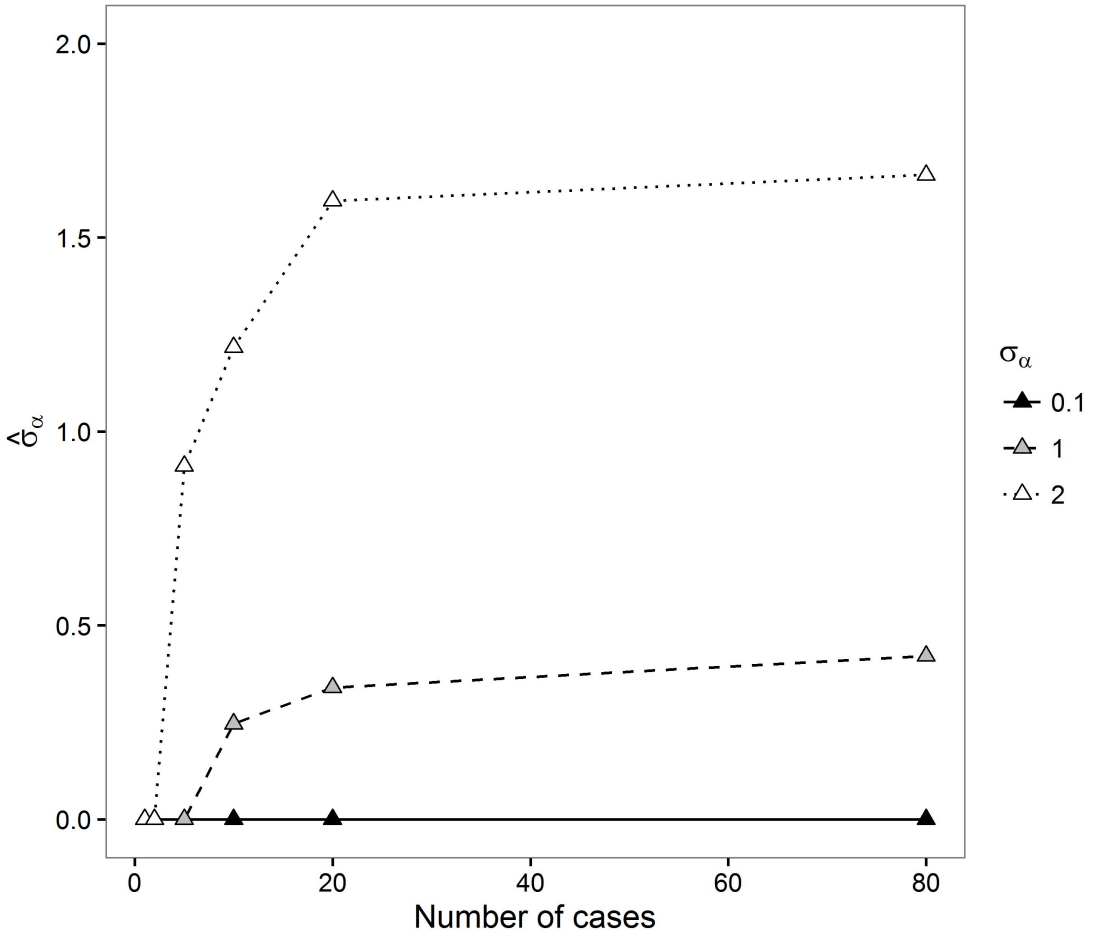

FIGURE 3.12: Estimates of σ_α from a matched case-control design with $n = 30$ fit using a marginal logistic model (MLM) with varying numbers of cases (c) and ratio of cases to controls equal to 0.5.

CHAPTER 4

Discussion

In this thesis, we illustrated the differences in parameter estimates between conditional logistic regression and mixed-effects logistic regression approaches for matched case-control data. Simulations confirmed that using the MLM results in biased parameter estimates and confidence intervals that did not achieve nominal coverage rates, except when the number of cases is large and clusters are relatively homogeneous (i.e., small σ_α). Furthermore, increasing the number of clusters had little effect on the bias, consistent with previous studies (Lubin, 1981; Craiu et al., 2011). Except for large cluster sizes, this bias was substantial. For example, consider the data set with observations of 5 used sites and 25 unused sites (i.e., $r = 0.2, c = 5$) from each of $n = 30$ animals. If $\sigma_\alpha = 1$ and $\beta_p = 1$, then the bias in the estimated odds (e^β) for the covariate was, on average, -27% for SCC and 10% for MLM, whereas the bias for CLM was <1%. Biases on the observed order of 10-30% could be problematic when trying to understand resource selection for sensitive species. Although remote sensing may allow for large cluster sizes encompassing thousands of observations (e.g., Johnson et al. 2004; Gillies et al. 2006), RSF studies often involve fewer, small clusters (Thomas and Taylor, 2006).

The bias of SCC was positive, consistent with previous studies for case-control designs with fine stratification (Lubin, 1981). Pike et al. (1980) showed that for clusters comprised of one case and one control, and with an indicator variable as the sole covariate, the quantity estimated is actually 2β. Consistent with Lubin (1981), we found that the number of cases should be at least 20 to substantially reduce the bias from SCC. However, the bias tended to be higher than for MLM, and SCC also had slightly higher rates of convergence failure. This indicates that MLM may provide a more stable approximation to the stratified case-control likelihood function than SCC.

The bias observed for MLM was consistent with the attenuation observed in other marginal logistic models. When averaging over individual-specific effects in the MLM, the population-level logistic function is less steep than for the individuals (Diggle

et al., 1998). This results in parameter values that are closer to zero for the population mean. In addition to biased population-level estimates from MLM, care must also be taken when making inferences about individual or cluster-specific effects. For example, Hebblewhite and Merrill (2008) suggests using estimated random effects from logistic regression models in a hierarchical setting to evaluate the relationship between resource selection and fitness. However, as indicated by our simulation studies, neglecting to incorporate the sampling design into the model causes variance components (i.e., σ_α) to be underestimated. This will, in turn, attenuate the estimates of the random effects. Intuitively, using MLM instead of CLM results in bias because a fixed number of observations from a single cluster are dependent, and hence their variance is lower than if the number of observed sites were random. Without accounting for this dependency in the model, the variance components will be underestimated. As shown in Chapter 2, there is no statistical justification to use MLM for matched case-control data. Since the MLM likelihood function is not a correct likelihood function for the data, likelihood-based values, such as Akaike's Information Criterion (Akaike, 1973; Burnham and Anderson, 2002) used for model selection, may be of questionable value.

Conditional logistic models provided the least biased estimates of $\boldsymbol{\beta}$, except when clusters were very small (i.e., one case and two controls) or very large (i.e., 80 cases and 800 controls). For both of these scenarios, convergence failure (a numerical problem) led to no or poor estimates. For small clusters, one option would be to increase the number of controls sampled, if increasing the number of cases was impossible. Compared to $r = 0.5$, decreasing the ratio to $r = 0.1$, even for a single observed case, improved convergence and bias for CLM. If neither the number of cases nor controls can be increased, an alternative may be to use a paired logistic model (i.e., 1:1 matching of cases and controls; Compton et al. 2002). For large clusters, numerical instability may have resulted from evaluating the sum in the denominator of Equation 2.10. For example, in the $c = 80, r = 0.1$ scenario, there are $u = \binom{880}{80} \approx 1.2 \times 10^{115}$ terms in the denominator of the likelihood function for a single animal. Numerical instability may occur when σ_α is large and there are many clusters (i.e., $n = 100$). However, for clusters of this size, MLM performed well as

long as the variance of the random effect was low. Therefore, MLM may be a viable alternative to CLM for very large clusters, though variance components will likely be negatively biased.

Complex model building and extensions of models for matched case-control data, such as the suggestion to incorporate random effects for the slope parameters, should be undertaken with care. Gillies et al. (2006) suggested that MLMs with random slopes can provide insight into functional responses in RSFs for matched case-control data. They extend the model with a single random intercept (α) in Equation 2.12 to include a random slope parameter for each individual. If we let γ denote the random effect for the habitat covariate for each individual, and specify the joint distribution of α and γ be $F(\alpha, \gamma)$, then the likelihood function for the i-th individual is given by

$$\mathcal{L}_i(\beta) = \iint \prod_{j=1}^{m_i} \frac{e^{y_{ij}[\alpha+(\beta+\gamma)x_{ij}]}}{1+e^{[\alpha+(\beta+\gamma)x_{ij}]}} dF(\alpha, \gamma). \tag{4.1}$$

As with the MLM for a single random effect (Equation 2.12), Equation 4.1 is based on an incorrect prospective likelihood function. Despite this, the approach has been adopted by a number of researchers (Boyce et al., 2003; Hebblewhite and Merrill, 2008).

Duchesne et al. (2010) and Craiu et al. (2011) described appropriate mixed-effects models for matched case-control data based on the conditional logistic likelihood function. The simplest case is a mixed-effects conditional logistic model with a random intercept only, which is motivated by considering the cluster-specific effects $\boldsymbol{\alpha}' = (\alpha_1, \alpha_2, \ldots, \alpha_n)$ to be drawn independently from a distribution, such as $\alpha_i \sim Normal(0, \sigma_\alpha)$. Then the contribution of the i-th cluster to the mixed-effects conditional likelihood function (from Equation 2.8) is given by

$$\mathcal{L}_i(\beta) = \frac{\int \prod_{j \in S} \frac{e^{\alpha+\beta x_j}}{1+e^{\alpha+\beta x_j}} \times \prod_{j \notin S} \frac{1}{1+e^{\alpha+\beta x_j}} dF(\alpha)}{\int \sum_{z=1}^{u} \left\{ \prod_{j \in S_z} \frac{e^{\alpha+\beta x_j}}{1+e^{\alpha+\beta x_j}} \times \prod_{j \notin S_z} \frac{1}{1+e^{\alpha+\beta x_j}} \right\} dF(\alpha)}. \tag{4.2}$$

Additional random effects can be specified for the other parameters, such as a random slope as suggested by Gillies et al. (2006). We let α be the cluster-specific intercepts and γ be the random effects for the habitat covariate for each individual with the joint distribution $F(\alpha, \gamma)$. Then, integrating over the distribution of each random effect, the likelihood function is given by

$$\mathcal{L}_i(\beta) = \frac{\iint \prod_{j \in S} \frac{e^{\alpha+(\beta+\gamma)x_j}}{1+e^{\alpha+(\beta+\gamma)x_j}} \times \prod_{j \notin S} \frac{1}{1+e^{\alpha+(\beta+\gamma)x_j}} dF(\alpha, \gamma)}{\iint \sum_{z=1}^{u} \left\{ \prod_{j \in S_z} \frac{e^{\alpha+(\beta+\gamma)x_j}}{1+e^{\alpha+(\beta+\gamma)x_j}} \times \prod_{j \notin S_z} \frac{1}{1+e^{\alpha+(\beta+\gamma)x_j}} \right\} dF(\alpha, \gamma)}, \tag{4.3}$$

which is not equivalent to the likelihood function proposed by (Gillies et al. 2006; Equation 4.1). The estimation of model parameters in Equation 4.3 is challenging because of the high dimensional integrals contributed by each of the clusters. Some estimation procedures have been proposed, including generalized estimating equations (Craiu et al., 2008) and a two-step procedure involving an expectation-maximization algorithm to implement restricted maximum likelihood estimation (Craiu et al., 2011)). Estimation of mixed conditional logistic models remains an area of active research (Duchesne et al., 2010). However, given the bias associates with the estimation of a single variance component (σ_α) using MLM, accurate estimation of multiple variance components seems challenging, especially for a small number of clusters (e.g., $n \leq 30$).

Our work illustrates the need for caution and deeper understanding of model development before extending or increasing the complexity of existing models. The use MLMs in place of the correct CLM resulted from misunderstanding about the use of PLM for case-control data. Appropriate management of natural resources requires careful inference from models and data (Holden and Ellner, 2016).

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APPENDIX A

Supplementary Information to Chapter 3

rejection sampler for matched case-control data

The following code corresponds the rejection sampler described in Chapter 3. The code is written for a more general implementation that can include fixed and random effects for the intercept and the slope, in addition to multiple fixed-effect slope parameters. The first section is the implementation in C. The second section of code provides the R commands to call and compile the code.

C Code for Rejection Sampler

```
/*C Rejection Sampler to generate matched case-control data*/

#include <stdlib.h>
#include <math.h>
#include <R.h>
#include <Rmath.h>

double g(double x)
{
return 1.0/(1.0 + exp(-x));
}

/* Function to simulate a case control study with n strata (clusters),
 * mcase cases per strata, and mcont controls per strata. The model for
 * the unconditional probability is
 *
 *  p_ij = g[beta_0 + zeta_0i + (beta_1 + zeta_1i)*x_ij1
 *         + beta_2*x_ij2 + beta_3*x_ij3]
 *
 * The marginal distribution of each x_ijk is U(-2,2), and
 * the x_ijk's are assumed to be independent.
 */

void casecontrol2(int *n, int *mcase, int *mcont,
double *beta, double *sigm, double *x1, double *x2, double *x3, double *y)
{
```

```
double beta0 = beta[0], beta1 = beta[1], beta2 = beta[2], beta3 = beta[3];
double sigm0 = sigm[0], sigm1 = sigm[1];
double ytmp, x1tmp, x2tmp, x3tmp, zeta0, zeta1;
int i, j, t = 0;

  GetRNGstate();

for (i = 0; i < *n; i++) {
    zeta0 = rnorm(0.0, sigm0);
    zeta1 = rnorm(0.0, sigm1);
for (j = 0; j < *mcase; j++) {
do {
x1tmp = runif(-2.0, 2.0);
x2tmp = runif(-2.0, 2.0);
x3tmp = runif(-2.0, 2.0);
ytmp = rbinom(1, g(beta0 + zeta0 + (beta1 + zeta1) * x1tmp
       + beta2 * x2tmp + beta3 * x3tmp));
} while (ytmp != 1.0);
y[t] = ytmp;
x1[t] = x1tmp;
x2[t] = x2tmp;
x3[t] = x3tmp;
++t;
}
for (j = 0; j < *mcont; j++) {
do {
x1tmp = runif(-2.0, 2.0);
x2tmp = runif(-2.0, 2.0);
x3tmp = runif(-2.0, 2.0);
ytmp = rbinom(1, g(beta0 + zeta0 + (beta1 + zeta1) * x1tmp
       + beta2 * x2tmp + beta3 * x3tmp));
} while (ytmp != 0.0);
y[t] = ytmp;
x1[t] = x1tmp;
x2[t] = x2tmp;
x3[t] = x3tmp;
++t;
}
}

PutRNGstate();
}
```

R Code for Rejection Sampler

```
# R code to call and compile C rejection sampler

system("R CMD SHLIB casecontrol2.c")

# Model:
# logit(Y_{ij}) = beta_0 + zeta_{0i} + (beta_1 + zeta_{1i})*x_{ij1}
        + beta_2*x_{ij2} + beta_3*x_{ij3}
# zeta_{0i} ~ N(0,sigma_1), zeta_{1i} ~ N(0,sigma_2)
# n = number of clusters
# m.case = number of cases
# m.cont = number of controls

# Note: Not set up to include random slopes for any of the new slopes.


casecontrol2 <- function(n, m.case, m.cont, beta = c(0, 1, 2, 3), sigm = c(1,0))
{
  if (!is.loaded("casecontrol2")) {
    dyn.load("casecontrol2")
  }
  if (as.integer(n) < 1) stop("n < 1")
  if (as.integer(m.case < 1)) stop("m.case < 1")
  if (as.integer(m.cont < 1)) stop("m.cont < 1")
  if (any(sigm < 0)) stop("sigm < 0")
  y  <- rep(0, n * (m.case + m.cont))
  x1 <- rep(0, n * (m.case + m.cont))
  x2 <- rep(0, n * (m.case + m.cont))
  x3 <- rep(0, n * (m.case + m.cont))
  tmp <- .C("casecontrol2",
    n = as.integer(n),
    m.case = as.integer(m.case),
    m.cont = as.integer(m.cont),
    beta = as.double(beta), sigm = as.double(sigm),
    x1 = as.double(x1),
    x2 = as.double(x2),
    x3 = as.double(x3),
    y  = as.double(y))
  return(data.frame(y = tmp$y, x1 = tmp$x1, x2 = tmp$x2, x3 = tmp$x3,
    cluster = factor(rep(1:n, each = m.case + m.cont))))
}
```

REJECTION SAMPLER PROOF

In this section, we demonstrate that the sampler used to generate matched case-control data (Appendix A.1) is a special case of the Accept-Reject method (Robert and Casella, 2013), and therefore samples the correct conditional distribution. In the standard rejection algorithm, $f(x)$ is the target distribution and $g(x)$ is the proposal distribution. The algorithm for the standard algorithm (Robert and Casella, 2013) is:

Begin Algorithm

Step 1. Simulate $x^* \sim g(x)$

Step 2. Calculate the acceptance ratio:

$$\alpha = \frac{f(x^*)}{k \cdot g(x^*)},$$

where $f(x^*)$ and $g(x^*)$ are the likelihoods evaluated at x^* for the target and proposal distributions, respectively, and $k \geqslant \sup_z \left\{ \frac{f(z)}{g(z)} \right\}$ is a constant.

Step 3. If $\alpha > u^* \sim \text{Uniform}(0,1)$, accept x^* as drawn from $f(x)$, else return to 1.

End Algorithm.

For the rejection sampler in Appendix A.1, we assume that probabilities of use, $p_{ij} = e^{\alpha_i + \beta x_{ij}} / (1 + e^{\alpha_i + \beta x_{ij}})$, are given. The target distribution is the logistic model, conditional on the number of used and unused sites in $\mathbf{y}$, which is given by $f(\mathbf{y}|\mathbf{p}, m, c)$. The proposal distribution is the unconditional model, $g(\mathbf{y}|\mathbf{p})$. That is, the model not constrained by the number of used and unused sites in each cluster (i.e., m and c). As in Chapter 2, we define:

$$f(\mathbf{y}|\mathbf{p}, m, c) = \prod_{j \in S} p_{ij} \times \prod_{j \notin S} (1 - p_{ij}), \tag{A.1}$$

and

$$g(\mathbf{y}|\mathbf{p}) = \sum_{z=1}^{u} \prod_{j \in S} p_{ij} \times \prod_{j \notin S} (1 - p_{ij}), \tag{A.2}$$

where S is the set of indices of the used locations and u is the number of possible assignments of c used locations among m observations.

Assume we propose $\mathbf{y}^*$ from $g(\mathbf{y}|\mathbf{p})$. We let the set of indices corresponding to $\mathbf{y}^*$ be S^*. If $S^* \not\equiv S$, then the target likelihood evaluated at $\mathbf{y}^*$ will be $f(\mathbf{y}^*|\mathbf{p}, m, c) = 0$, since f is only defined on S. The acceptance ratio in this case is

$$\alpha = \frac{f(\mathbf{y}^*|\mathbf{p}, m, c)}{k \cdot g(\mathbf{y}^*|\mathbf{p})} = 0, \tag{A.3}$$

which is always less than or equal to $u^* \sim \text{Uniform}(0, 1)$. Therefore, if $S^* \not\equiv S$, the proposals are always rejected. If $S^* \equiv S$, then we note that $f(\mathbf{y}^*|\mathbf{p}, m, c) = g(\mathbf{y}^*|\mathbf{p})$, and that

$$k \geqslant \sup_{\mathbf{z}} \left\{ \frac{f(\mathbf{z}|\mathbf{p}, m, c)}{g(\mathbf{z}|\mathbf{p})} \right\} = 1, \tag{A.4}$$

since f and g conditional on $S^* \equiv S$ are the same model. The acceptance ratio in this case, choosing c= 1, is

$$\alpha = \frac{f(\mathbf{y}^*|\mathbf{p}, m, c)}{1 \cdot g(\mathbf{y}^*|\mathbf{p})} = 1, \tag{A.5}$$

which is always greater than or equal to $u^* \sim \text{Uniform}(0, 1)$. So if $S^* \equiv S$, proposals are always accepted.

APPENDIX B

Supplementary Information to Chapter 3

CODE FOR SIMULATION STUDY

This section provides the wrappers for R functions to fit prospective logistic models (PLM), stratified case-control models (SCC), marginal logistic models (MLM), and conditional logistic models (CLM) to data generated using the rejection sampler in Appendix A.

Wrappers for Model Fitting

```
### Description
# This group of functions takes the data from casecontrol()
# [x, y, and cluster] and fits a fixed effects logistic
# regression model ("glm"), a mixed effects logistic
# regression model with a random intercept ("glmer1") or
# random intercept and random slope ("glmer2), or a
# conditional logistic regression model without a
# random slope ("clogit").

# The get.() functions fit the models and return parameter
# values. tryCatch.W.E. handles warnings and stores them
# in a list element $warning, and returns NA if an error
# occurred.

# fit.safe() combines both functions, using switch() to
# specify the desired method. It returns a list with the
# parameter estimates in $value and any warnings in $warning.

require(lme4)
require(survival)


#  Functions to get the results ------------------------------

get.glm.2 = function(data){
  model = glm(y ~ x1 + x2 + x3, data = data, family = binomial)
  results = data.frame(b0 = coef(model)[1],
```

```
                        b1 = coef(model)[2],
                        b2 = coef(model)[3],
                        b3 = coef(model)[4],
                        b0.SE = sqrt(diag(vcov(model)))[1],
                        b1.SE = sqrt(diag(vcov(model)))[2],
                        b2.SE = sqrt(diag(vcov(model)))[3],
                        b3.SE = sqrt(diag(vcov(model)))[4],
                        method = "glm", row.names = NULL)
  return(results)
}

get.glm.int.2 = function(data){
  model = glm(y ~ x1 + x2 + x3 + cluster, data = data,
              family = binomial)
  results = data.frame(b0 = coef(model)[1],
                        b1 = coef(model)[2],
                        b2 = coef(model)[3],
                        b3 = coef(model)[4],
                        b0.SE = sqrt(diag(vcov(model)))[1],
                        b1.SE = sqrt(diag(vcov(model)))[2],
                        b2.SE = sqrt(diag(vcov(model)))[3],
                        b3.SE = sqrt(diag(vcov(model)))[4],
                        method = "glm.int", row.names = NULL)
  return(results)
}

get.glmer1.2 = function(data){
  model = glmer(y ~ x1 + x2 + x3 + (1 |cluster),
                data = data, family = binomial)
  results = data.frame(b0 = fixef(model)[1],
                        b1 = fixef(model)[2],
                        b2 = fixef(model)[3],
                        b3 = fixef(model)[4],
                        b0.SE = sqrt(diag(vcov(model)))[1],
                        b1.SE = sqrt(diag(vcov(model)))[2],
                        b2.SE = sqrt(diag(vcov(model)))[3],
                        b3.SE = sqrt(diag(vcov(model)))[4],
                        s1 = as.data.frame(VarCorr(model))$vcov[1],
                        method = "glmer1", row.names = NULL)
  return(results)
}

get.glmer2.2 = function(data){
  model = glmer(y ~ x1 + x2 + x3 + (1 + x1|cluster),
                data = data, family = binomial)
```

```
  results = data.frame(b0 = fixef(model)[1],
                       b1 = fixef(model)[2],
                       b2 = fixef(model)[3],
                       b3 = fixef(model)[4],
                       b0.SE = sqrt(diag(vcov(model)))[1],
                       b1.SE = sqrt(diag(vcov(model)))[2],
                       b2.SE = sqrt(diag(vcov(model)))[3],
                       b3.SE = sqrt(diag(vcov(model)))[4],
                       s1 = as.data.frame(VarCorr(model))$vcov[1],
                       s2 = as.data.frame(VarCorr(model))$vcov[2],
                       method = "glmer2", row.names = NULL)
  return(results)
}

get.clogit.2 = function(data){
  model = clogit(y ~ x1 + x2 + x3 + strata(cluster),
                 data = data)
  results = data.frame(b1 = coef(model)[1],
                       b2 = coef(model)[2],
                       b3 = coef(model)[3],
                       b1.SE = sqrt(diag(vcov(model)))[1],
                       b2.SE = sqrt(diag(vcov(model)))[2],
                       b3.SE = sqrt(diag(vcov(model)))[3],
                       method = "clogit", row.names = NULL)
  return(results)
}


# Function for error handling ---------------------------------

tryCatch.W.E <- function(expr){
  W <- NA
  w.handler <- function(w){ # warning handler
    W <<- w                         # store the warning message
    invokeRestart("muffleWarning")
  }
  list(value = withCallingHandlers(tryCatch(expr, error = function(e) NA),
               warning = w.handler),warning = W)
}


# Combined fit safe function ----------------------------------

fit.safe2 = function(data = data, type = NULL){
  switch(type,
```

```
          glm = tryCatch.W.E(get.glm.2(data)),
          glm.int = tryCatch.W.E(get.glm.int.2(data)),
          glmer1 = tryCatch.W.E(get.glmer1.2(data)),
          glmer2 = tryCatch.W.E(get.glmer2.2(data)),
          clogit = tryCatch.W.E(get.clogit.2(data))
  )
}
```

Fit Models and Format Data

```
# Simulations for "ordered" series of plots.
# Use a model with three slope parameters.

set.seed(100)
source("clogit2.R")
source("fit_safe_function2.R")
require(plyr)

# Parameter value summary:
#         c = 1, 2, 5, 10
#   (m - c) = c/(0.5, 0.2, and 0.1)
#         n = 100 or 30
#  beta_vec = 0, 1, 2, 3
#      sig1 = 0.1, 1, 2
#      sig2 = 0

# Import parameter values
parm_vals_031916 = read.csv("parm_vals_031916.csv")


# Small number of clusters ------------------------------------------------
parm_vals_031916$n = 30

### Expand the parameter values by reps
reps = 150  # Number of simulations
parms = data.frame(sapply(parm_vals_031916, rep.int, times = reps))

### Generate the datasets
data1 = lapply(seq_along(1:nrow(parms)),
               function(i){casecontrol2(n = parms$n[i],
                                        m.case = parms$cases[i],
                                        m.cont = parms$controls[i],
                                        sigm = parms[i, c("s1", "s2")])})


### Fit glm, glm.int, glmer1, and clogit
results1 = lapply(data1, function(x) fit.safe2(x, "glm"))
results4 = lapply(data1, function(x) fit.safe2(x, "glm.int"))
results2 = lapply(data1, function(x) fit.safe2(x, "glmer1"))
results3 = lapply(data1, function(x) fit.safe2(x, "clogit"))


### Format results
```

```
# glm
glm_error_parms = parms[is.na(sapply(results1, "[", "value")), ]
write.csv(glm_error_parms, "lown_glm_error_parms.csv")
results1_drop = results1[is.na(sapply(results1, "[", "value"))==F]
parms_drop = parms[is.na(sapply(results1, "[", "value"))==F, ]

glm_res = ldply(results1_drop, "[[", "value")
glm_res$warn = ifelse(is.na(sapply(results1_drop,
               "[[", "warning")), FALSE, TRUE)
glm_out = data.frame(parms_drop, glm_res)
write.csv(glm_out, "lown_glm_out.csv")



# glm.int
glm.int_error_parms = parms[is.na(sapply(results4, "[", "value")), ]
write.csv(glm.int_error_parms, "lown_glmint_error_parms.csv")
results4_drop = results4[is.na(sapply(results4, "[", "value"))==F]
parms_drop = parms[is.na(sapply(results4, "[", "value"))==F, ]

glm.int_res = ldply(results4_drop, "[[", "value")
glm.int_res$warn = ifelse(is.na(sapply(results4_drop,
                   "[[", "warning")), FALSE, TRUE)
glm.int_out = data.frame(parms_drop, glm.int_res)
write.csv(glm.int_out, "lown_glmint_out.csv")



# glmer
glmer_error_parms = parms[is.na(sapply(results2, "[", "value")), ]
write.csv(glmer_error_parms, "lown_glmer_error_parms.csv")
results2_drop = results2[is.na(sapply(results2, "[", "value"))==F]
parms_drop = parms[is.na(sapply(results2, "[", "value"))==F, ]

glmer1_res = ldply(results2_drop, "[[", "value")
glmer1_res$warn = ifelse(is.na(sapply(results2_drop,
                  "[[", "warning")), FALSE, TRUE)
glmer1_out = data.frame(parms_drop, glmer1_res)
write.csv(glmer1_out, "lown_glmer1_out.csv")



#clogit
clogit_error_parms = parms[is.na(sapply(results3, "[", "value")), ]
write.csv(clogit_error_parms, "lown_clogit_error_parms.csv")
```

```
results3_drop = results3[is.na(sapply(results3, "[", "value"))==F]
parms_drop3 = parms[is.na(sapply(results3, "[", "value"))==F,]

clogit_res = ldply(results3_drop, "[[", "value")
clogit_res$warn = ifelse(is.na(sapply(results3_drop,
                  "[[", "warning")), FALSE, TRUE)
clogit_out = data.frame(parms_drop3, clogit_res)
write.csv(clogit_out, "lown_clogit_out.csv")



# Large number of clusters ------------------------------------------------
parm_vals_031916$n = 100

### Expand the parameter values by reps
reps = 150
parms = data.frame(sapply(parm_vals_031916, rep.int, times = reps))

### Generate the datasets
data1 = lapply(seq_along(1:nrow(parms)),
               function(i){casecontrol2(n = parms$n[i],
                                        m.case = parms$cases[i],
                                        m.cont = parms$controls[i],
                                        sigm = parms[i, c("s1", "s2")])})



### Fit glm, glmer1, and clogit

results1 = lapply(data1, function(x) fit.safe2(x, "glm"))
results4 = lapply(data1, function(x) fit.safe2(x, "glm.int"))
results2 = lapply(data1, function(x) fit.safe2(x, "glmer1"))
results3 = lapply(data1, function(x) fit.safe2(x, "clogit"))


### Format results
# glm
glm_error_parms = parms[is.na(sapply(results1, "[", "value")), ]
write.csv(glm_error_parms, "bign_glm_error_parms.csv")
results1_drop = results1[is.na(sapply(results1, "[", "value"))==F]
parms_drop = parms[is.na(sapply(results1, "[", "value"))==F, ]

glm_res = ldply(results1_drop, "[[", "value")
glm_res$warn = ifelse(is.na(sapply(results1_drop,
               "[[", "warning")), FALSE, TRUE)
```

```
glm_out = data.frame(parms_drop, glm_res)
write.csv(glm_out, "bign_glm_out.csv")



# glm.int
glm.int_error_parms = parms[is.na(sapply(results4, "[", "value")), ]
write.csv(glm.int_error_parms, "bign_glmint_error_parms.csv")
results4_drop = results4[is.na(sapply(results4, "[", "value"))==F]
parms_drop = parms[is.na(sapply(results4, "[", "value"))==F, ]

glm.int_res = ldply(results4_drop, "[[", "value")
glm.int_res$warn = ifelse(is.na(sapply(results4_drop,
                   "[[", "warning")), FALSE, TRUE)
glm.int_out = data.frame(parms_drop, glm.int_res)
write.csv(glm.int_out, "bign_glmint_out.csv")




# glmer
glmer_error_parms = parms[is.na(sapply(results2, "[", "value")), ]
write.csv(glmer_error_parms, "bign_glmer_error_parms.csv")
results2_drop = results2[is.na(sapply(results2, "[", "value"))==F]
parms_drop = parms[is.na(sapply(results2, "[", "value"))==F, ]

glmer1_res = ldply(results2_drop, "[[", "value")
glmer1_res$warn = ifelse(is.na(sapply(results2_drop, "[[", "warning")), FALSE, TRUE)
glmer1_out = data.frame(parms_drop, glmer1_res)
write.csv(glmer1_out, "bign_glmer1_out.csv")



#clogit
clogit_error_parms = parms[is.na(sapply(results3, "[", "value")), ]
write.csv(clogit_error_parms, "bign_clogit_error_parms.csv")
results3_drop = results3[is.na(sapply(results3, "[", "value"))==F]
parms_drop3 = parms[is.na(sapply(results3, "[", "value"))==F,]

clogit_res = ldply(results3_drop, "[[", "value")
clogit_res$warn = ifelse(is.na(sapply(results3_drop,
                  "[[", "warning")), FALSE, TRUE)
clogit_out = data.frame(parms_drop3, clogit_res)
write.csv(clogit_out, "bign_clogit_out.csv")
```

APPENDIX C

Supplementary Information to Chapter 3

simulation results for $n = 100$

Table C.1: Estimated bias and Monte Carlo standard errors estimated from simulations with $n = 100$. The model included three slope parameters (β_p). Simulations varied the number of cases (c), the ratio of cases to controls (r), and the magnitude of the variance of the individual-specific random effect (σ_α). Models used were the prospective logistic model (PLM), stratified case-control model (SCC), marginal logistic model (MLM), and the conditional logistic model (CLM). Empty cells indicate complete convergence failure for the given model and simulation parameter values. Superscripts indicate the exponents of scientific notation.

c	r	β_p	σ_α	PLM	SE	SCC	SE	MLM	SE	CLM	SE
1	0.1	1	1.0	-7.3^{-2}	1.3^{-2}	0.53	2.7^{-2}	-7.3^{-2}	1.3^{-2}	3.9^{-2}	1.8^{-2}
1	0.1	1	2.0	-2.4^{-1}	1.2^{-2}	0.55	2.5^{-2}	-2.3^{-1}	1.3^{-2}	5.2^{-2}	1.7^{-2}
1	0.1	2	0.1	4.4^{-2}	1.9^{-2}	1.07	3.5^{-2}	4.4^{-2}	1.9^{-2}	9.5^{-2}	2.7^{-2}
1	0.1	2	1.0	-1.6^{-1}	1.7^{-2}	1.02	3.6^{-2}	-1.6^{-1}	1.7^{-2}	5.5^{-2}	2.5^{-2}
1	0.1	2	2.0	-4.7^{-1}	1.5^{-2}	1.09	3.5^{-2}	-4.5^{-1}	1.5^{-2}	8.3^{-2}	2.2^{-2}
1	0.1	3	0.1	3.9^{-2}	2.4^{-2}	1.56	4.9^{-2}	3.9^{-2}	2.4^{-2}	1.0^{-1}	3.2^{-2}
1	0.1	3	1.0	-2.2^{-1}	2.1^{-2}	1.57	5.1^{-2}	-2.2^{-1}	2.1^{-2}	1.2^{-1}	3.4^{-2}
1	0.1	3	2.0	-7.1^{-1}	1.7^{-2}	1.63	4.8^{-2}	-6.8^{-1}	1.8^{-2}	1.3^{-1}	2.9^{-2}
1	0.2	1	0.1	2.5^{-2}	1.6^{-2}	0.65	3.4^{-2}	2.5^{-2}	1.6^{-2}	8.2^{-2}	2.3^{-2}
1	0.2	1	1.0	-6.7^{-2}	1.4^{-2}	0.67	3.3^{-2}	-6.7^{-2}	1.4^{-2}	6.0^{-2}	2.3^{-2}
1	0.2	1	2.0	-2.7^{-1}	1.4^{-2}	0.57	3.7^{-2}	-2.7^{-1}	1.4^{-2}	2.0^{-3}	2.4^{-2}
1	0.2	2	0.1	5.2^{-2}	2.1^{-2}	1.37	4.7^{-2}	5.2^{-2}	2.1^{-2}	1.6^{-1}	3.3^{-2}
1	0.2	2	1.0	-1.6^{-1}	1.9^{-2}	1.33	4.4^{-2}	-1.6^{-1}	1.9^{-2}	1.3^{-1}	3.6^{-2}
1	0.2	2	2.0	-4.8^{-1}	1.6^{-2}	1.30	4.7^{-2}	-4.8^{-1}	1.7^{-2}	8.1^{-2}	3.0^{-2}
1	0.2	3	0.1	7.9^{-2}	2.9^{-2}	2.08	7.3^{-2}	7.9^{-2}	2.9^{-2}	2.6^{-1}	4.7^{-2}
1	0.2	3	1.0	-2.0^{-1}	2.4^{-2}	2.06	5.9^{-2}	-2.0^{-1}	2.4^{-2}	2.1^{-1}	4.4^{-2}
1	0.2	3	2.0	-7.2^{-1}	2.1^{-2}	1.93	6.6^{-2}	-7.2^{-1}	2.2^{-2}	1.3^{-1}	4.4^{-2}
1	0.5	1	0.1	4.0^{-2}	2.3^{-2}	0.80	5.7^{-2}	4.0^{-2}	2.3^{-2}	1.6^{-1}	5.4^{-2}

Table C.1 continued

1	0.1	1	0.1	2.9^{-2}	1.4^{-2}	0.54	2.6^{-2}	2.9^{-2}	1.4^{-2}	4.2^{-2}	1.8^{-2}
1	0.5	1	1.0	-6.6^{-2}	1.8^{-2}	0.82	5.6^{-2}	-6.6^{-2}	1.8^{-2}	1.8^{-1}	4.9^{-2}
1	0.5	1	2.0	-2.4^{-1}	1.6^{-2}	0.74	5.5^{-2}	-2.4^{-1}	1.6^{-2}	2.5^{-1}	7.7^{-2}
1	0.5	2	0.1	6.0^{-2}	2.7^{-2}	1.59	7.1^{-2}	6.0^{-2}	2.7^{-2}	2.5^{-1}	6.3^{-2}
1	0.5	2	1.0	-1.1^{-1}	2.4^{-2}	1.72	7.5^{-2}	-1.1^{-1}	2.4^{-2}	3.3^{-1}	7.0^{-2}
1	0.5	2	2.0	-4.6^{-1}	1.8^{-2}	1.55	6.1^{-2}	-4.6^{-1}	1.8^{-2}	5.1^{-1}	1.6^{-1}
1	0.5	3	0.1	1.1^{-1}	3.8^{-2}	2.51	9.1^{-2}	1.1^{-1}	3.8^{-2}	4.7^{-1}	1.0^{-1}
1	0.5	3	1.0	-1.9^{-1}	2.7^{-2}	2.56	7.8^{-2}	-1.9^{-1}	2.7^{-2}	4.6^{-1}	9.1^{-2}
1	0.5	3	2.0	-7.0^{-1}	2.3^{-2}	2.37	7.8^{-2}	-7.0^{-1}	2.3^{-2}	7.6^{-1}	2.1^{-1}
2	0.1	1	0.1	1.1^{-2}	9.4^{-3}	0.27	1.3^{-2}	1.1^{-2}	9.4^{-3}	2.1^{-2}	1.0^{-2}
2	0.1	1	1.0	-7.7^{-2}	8.4^{-3}	0.26	1.3^{-2}	-7.6^{-2}	8.4^{-3}	1.8^{-2}	9.4^{-3}
2	0.1	1	2.0	-2.5^{-1}	8.8^{-3}	0.26	1.5^{-2}	-1.4^{-1}	1.0^{-2}	7.8^{-3}	1.1^{-2}
2	0.1	2	0.1	4.1^{-2}	1.2^{-2}	0.57	2.0^{-2}	4.1^{-2}	1.2^{-2}	5.7^{-2}	1.4^{-2}
2	0.1	2	1.0	-1.7^{-1}	1.1^{-2}	0.51	2.1^{-2}	-1.7^{-1}	1.2^{-2}	1.5^{-2}	1.5^{-2}
2	0.1	2	2.0	-4.7^{-1}	9.2^{-3}	0.52	2.0^{-2}	-2.5^{-1}	1.3^{-2}	1.7^{-2}	1.4^{-2}
2	0.1	3	0.1	5.5^{-2}	1.5^{-2}	0.82	2.5^{-2}	5.5^{-2}	1.5^{-2}	7.1^{-2}	1.6^{-2}
2	0.1	3	1.0	-2.6^{-1}	1.5^{-2}	0.76	2.6^{-2}	-2.5^{-1}	1.5^{-2}	2.7^{-2}	1.8^{-2}
2	0.1	3	2.0	-7.1^{-1}	1.2^{-2}	0.77	2.8^{-2}	-3.8^{-1}	1.8^{-2}	3.1^{-2}	1.9^{-2}
2	0.2	1	0.1	1.6^{-2}	1.1^{-2}	0.38	1.8^{-2}	1.6^{-2}	1.1^{-2}	2.0^{-2}	1.2^{-2}
2	0.2	1	1.0	-7.0^{-2}	9.7^{-3}	0.38	1.7^{-2}	-7.0^{-2}	9.7^{-3}	2.8^{-2}	1.2^{-2}
2	0.2	1	2.0	-2.3^{-1}	9.6^{-3}	0.39	1.8^{-2}	-1.4^{-1}	1.1^{-2}	2.9^{-2}	1.2^{-2}
2	0.2	2	0.1	1.1^{-2}	1.6^{-2}	0.73	3.0^{-2}	1.1^{-2}	1.6^{-2}	2.3^{-2}	1.9^{-2}
2	0.2	2	1.0	-1.4^{-1}	1.3^{-2}	0.75	2.6^{-2}	-1.4^{-1}	1.3^{-2}	4.0^{-2}	1.8^{-2}
2	0.2	2	2.0	-4.7^{-1}	1.1^{-2}	0.80	2.8^{-2}	-3.0^{-1}	1.5^{-2}	6.4^{-2}	1.8^{-2}
2	0.2	3	0.1	3.7^{-2}	2.0^{-2}	1.12	3.7^{-2}	3.7^{-2}	2.0^{-2}	5.4^{-2}	2.2^{-2}
2	0.2	3	1.0	-2.4^{-1}	1.7^{-2}	1.10	3.7^{-2}	-2.4^{-1}	1.7^{-2}	4.8^{-2}	2.4^{-2}
2	0.2	3	2.0	-7.2^{-1}	1.3^{-2}	1.17	3.6^{-2}	-4.6^{-1}	1.8^{-2}	7.7^{-2}	2.2^{-2}
2	0.5	1	0.1	8.1^{-4}	1.4^{-2}	0.58	3.1^{-2}	8.1^{-4}	1.4^{-2}	2.3^{-2}	1.9^{-2}
2	0.5	1	1.0	-6.5^{-2}	1.4^{-2}	0.65	3.1^{-2}	-6.4^{-2}	1.4^{-2}	6.8^{-2}	1.9^{-2}
2	0.5	1	2.0	-2.3^{-1}	1.1^{-2}	0.64	2.7^{-2}	-2.0^{-1}	1.3^{-2}	6.4^{-2}	2.0^{-2}
2	0.5	2	0.1	2.3^{-2}	1.8^{-2}	1.18	3.9^{-2}	2.3^{-2}	1.8^{-2}	6.5^{-2}	2.4^{-2}
2	0.5	2	1.0	-1.2^{-1}	1.8^{-2}	1.27	4.4^{-2}	-1.2^{-1}	1.8^{-2}	1.1^{-1}	2.7^{-2}

Table C.1 continued

1	0.1	1	0.1	2.9^{-2}	1.4^{-2}	0.54	2.6^{-2}	2.9^{-2}	1.4^{-2}	4.2^{-2}	1.8^{-2}
2	0.5	2	2.0	-4.6^{-1}	1.3^{-2}	1.27	4.0^{-2}	-4.0^{-1}	1.5^{-2}	1.1^{-1}	2.4^{-2}
2	0.5	3	0.1	5.1^{-2}	2.4^{-2}	1.84	5.9^{-2}	5.1^{-2}	2.4^{-2}	1.3^{-1}	3.4^{-2}
2	0.5	3	1.0	-2.1^{-1}	2.3^{-2}	1.86	6.2^{-2}	-2.1^{-1}	2.3^{-2}	1.4^{-1}	3.8^{-2}
2	0.5	3	2.0	-7.1^{-1}	1.8^{-2}	1.88	5.3^{-2}	-6.2^{-1}	2.2^{-2}	1.5^{-1}	3.4^{-2}
5	0.1	1	0.1	-1.2^{-4}	5.6^{-3}	0.08	6.3^{-3}	-1.2^{-4}	5.6^{-3}	4.0^{-3}	5.7^{-3}
5	0.1	1	1.0	-7.4^{-2}	5.5^{-3}	0.09	6.7^{-3}	-3.7^{-2}	6.1^{-3}	1.3^{-2}	6.0^{-3}
5	0.1	1	2.0	-2.4^{-1}	5.5^{-3}	0.09	6.2^{-3}	-4.3^{-2}	5.6^{-3}	4.9^{-3}	5.6^{-3}
5	0.1	2	0.1	1.5^{-2}	7.6^{-3}	0.18	9.1^{-3}	1.5^{-2}	7.6^{-3}	2.2^{-2}	8.0^{-3}
5	0.1	2	1.0	-1.6^{-1}	7.9^{-3}	0.17	1.1^{-2}	-8.4^{-2}	9.1^{-3}	1.3^{-2}	9.4^{-3}
5	0.1	2	2.0	-4.7^{-1}	7.8^{-3}	0.17	9.6^{-3}	-8.1^{-2}	8.6^{-3}	1.0^{-2}	8.5^{-3}
5	0.1	3	0.1	2.2^{-2}	9.4^{-3}	0.27	1.2^{-2}	2.2^{-2}	9.4^{-3}	2.9^{-2}	1.0^{-2}
5	0.1	3	1.0	-2.4^{-1}	9.1^{-3}	0.26	1.4^{-2}	-1.3^{-1}	1.1^{-2}	2.3^{-2}	1.2^{-2}
5	0.1	3	2.0	-7.1^{-1}	9.1^{-3}	0.26	1.1^{-2}	-1.3^{-1}	1.0^{-2}	1.6^{-2}	9.8^{-3}
5	0.2	1	0.1	6.1^{-3}	7.5^{-3}	0.12	8.9^{-3}	6.1^{-3}	7.5^{-3}	6.2^{-3}	7.8^{-3}
5	0.2	1	1.0	-8.1^{-2}	6.1^{-3}	0.13	7.6^{-3}	-4.7^{-2}	6.4^{-3}	1.2^{-2}	6.5^{-3}
5	0.2	1	2.0	-2.5^{-1}	5.9^{-3}	0.11	8.6^{-3}	-6.1^{-2}	7.1^{-3}	-6.2^{-4}	7.4^{-3}
5	0.2	2	0.1	5.7^{-3}	9.8^{-3}	0.24	1.2^{-2}	5.7^{-3}	9.8^{-3}	9.4^{-3}	9.8^{-3}
5	0.2	2	1.0	-1.6^{-1}	8.4^{-3}	0.25	1.2^{-2}	-9.7^{-2}	9.6^{-3}	1.8^{-2}	1.0^{-2}
5	0.2	2	2.0	-5.1^{-1}	7.6^{-3}	0.23	1.2^{-2}	-1.2^{-1}	9.7^{-3}	-1.4^{-3}	9.9^{-3}
5	0.2	3	0.1	1.3^{-2}	1.2^{-2}	0.36	1.5^{-2}	1.3^{-2}	1.2^{-2}	1.8^{-2}	1.3^{-2}
5	0.2	3	1.0	-2.5^{-1}	1.1^{-2}	0.36	1.7^{-2}	-1.6^{-1}	1.3^{-2}	1.9^{-2}	1.4^{-2}
5	0.2	3	2.0	-7.6^{-1}	9.5^{-3}	0.35	1.6^{-2}	-1.8^{-1}	1.3^{-2}	5.4^{-3}	1.3^{-2}
5	0.5	1	0.1	1.7^{-2}	8.4^{-3}	0.21	1.1^{-2}	1.7^{-2}	8.4^{-3}	2.0^{-2}	8.4^{-3}
5	0.5	1	1.0	-7.4^{-2}	6.8^{-3}	0.21	1.1^{-2}	-5.8^{-2}	7.1^{-3}	1.8^{-2}	8.7^{-3}
5	0.5	1	2.0	-2.5^{-1}	7.1^{-3}	0.20	1.1^{-2}	-8.3^{-2}	8.3^{-3}	6.0^{-3}	8.6^{-3}
5	0.5	2	0.1	2.9^{-2}	1.1^{-2}	0.42	1.6^{-2}	2.9^{-2}	1.1^{-2}	3.3^{-2}	1.2^{-2}
5	0.5	2	1.0	-1.7^{-1}	1.0^{-2}	0.40	1.7^{-2}	-1.4^{-1}	1.1^{-2}	1.1^{-2}	1.3^{-2}
5	0.5	2	2.0	-5.0^{-1}	8.2^{-3}	0.41	1.5^{-2}	-1.5^{-1}	1.1^{-2}	2.0^{-2}	1.2^{-2}
5	0.5	3	0.1	4.3^{-2}	1.4^{-2}	0.63	2.1^{-2}	4.3^{-2}	1.4^{-2}	4.9^{-2}	1.5^{-2}
5	0.5	3	1.0	-2.5^{-1}	1.3^{-2}	0.61	2.3^{-2}	-2.0^{-1}	1.4^{-2}	3.0^{-2}	1.6^{-2}
5	0.5	3	2.0	-7.5^{-1}	1.1^{-2}	0.61	2.1^{-2}	-2.3^{-1}	1.4^{-2}	2.6^{-2}	1.5^{-2}

Table C.1 continued

1	0.1	1	0.1	2.9^{-2}	1.4^{-2}	0.54	2.6^{-2}	2.9^{-2}	1.4^{-2}	4.2^{-2}	1.8^{-2}
10	0.1	1	0.1	2.0^{-3}	4.3^{-3}	0.04	4.6^{-3}	2.0^{-3}	4.3^{-3}	2.5^{-3}	4.4^{-3}
10	0.1	1	1.0	-8.3^{-2}	4.2^{-3}	0.04	4.6^{-3}	-1.9^{-2}	4.4^{-3}	3.1^{-3}	4.4^{-3}
10	0.1	1	2.0	-2.4^{-1}	4.4^{-3}	0.04	5.0^{-3}	-2.0^{-2}	4.7^{-3}	1.2^{-3}	4.8^{-3}
10	0.1	2	0.1	2.8^{-4}	5.1^{-3}	0.07	5.4^{-3}	2.8^{-4}	5.1^{-3}	-6.5^{-4}	5.1^{-3}
10	0.1	2	1.0	-1.7^{-1}	5.6^{-3}	0.08	6.4^{-3}	-4.1^{-2}	6.0^{-3}	2.2^{-3}	6.0^{-3}
10	0.1	2	2.0	-4.8^{-1}	5.8^{-3}	0.09	5.4^{-3}	-2.9^{-2}	5.1^{-3}	1.4^{-2}	5.1^{-3}
10	0.1	3	0.1	7.3^{-4}	6.6^{-3}	0.11	7.1^{-3}	7.3^{-4}	6.6^{-3}	-2.6^{-4}	6.6^{-3}
10	0.1	3	1.0	-2.6^{-1}	7.4^{-3}	0.11	8.3^{-3}	-7.0^{-2}	7.7^{-3}	-2.3^{-3}	7.7^{-3}
10	0.1	3	2.0	-7.3^{-1}	8.1^{-3}	0.12	7.8^{-3}	-5.8^{-2}	7.3^{-3}	7.9^{-3}	7.3^{-3}
10	0.2	1	0.1	3.5^{-3}	4.7^{-3}	0.06	5.3^{-3}	3.5^{-3}	4.7^{-3}	5.3^{-3}	4.9^{-3}
10	0.2	1	1.0	-8.4^{-2}	4.2^{-3}	0.06	4.7^{-3}	-2.3^{-2}	4.4^{-3}	5.6^{-3}	4.4^{-3}
10	0.2	1	2.0	-2.5^{-1}	4.5^{-3}	0.05	5.4^{-3}	-2.8^{-2}	5.0^{-3}	-1.2^{-3}	5.1^{-3}
10	0.2	2	0.1	8.3^{-3}	6.7^{-3}	0.11	7.7^{-3}	8.3^{-3}	6.7^{-3}	1.1^{-2}	7.0^{-3}
10	0.2	2	1.0	-1.7^{-1}	5.4^{-3}	0.11	6.6^{-3}	-5.2^{-2}	5.9^{-3}	2.3^{-3}	6.0^{-3}
10	0.2	2	2.0	-4.8^{-1}	6.0^{-3}	0.11	6.9^{-3}	-4.7^{-2}	6.4^{-3}	5.5^{-3}	6.4^{-3}
10	0.2	3	0.1	1.3^{-2}	8.9^{-3}	0.17	1.0^{-2}	1.3^{-2}	8.9^{-3}	1.7^{-2}	9.4^{-3}
10	0.2	3	1.0	-2.7^{-1}	7.1^{-3}	0.16	8.8^{-3}	-8.1^{-2}	7.9^{-3}	1.4^{-3}	8.1^{-3}
10	0.2	3	2.0	-7.3^{-1}	7.5^{-3}	0.16	9.1^{-3}	-7.4^{-2}	8.2^{-3}	6.8^{-3}	8.3^{-3}
10	0.5	1	0.1	-4.5^{-3}	5.8^{-3}	0.08	6.4^{-3}	-4.5^{-3}	5.8^{-3}	-3.8^{-3}	5.8^{-3}
10	0.5	1	1.0	-9.5^{-2}	5.2^{-3}	0.08	6.2^{-3}	-4.4^{-2}	5.4^{-3}	-7.1^{-3}	5.6^{-3}
10	0.5	1	2.0	-2.5^{-1}	4.9^{-3}	0.09	6.1^{-3}	-3.3^{-2}	6.0^{-3}	9.3^{-3}	5.6^{-3}
10	0.5	2	0.1	1.2^{-2}	7.0^{-3}	0.18	8.1^{-3}	1.2^{-2}	7.0^{-3}	1.4^{-2}	7.1^{-3}
10	0.5	2	1.0	-1.7^{-1}	7.2^{-3}	0.18	8.8^{-3}	-6.3^{-2}	7.6^{-3}	1.3^{-2}	7.7^{-3}
10	0.5	2	2.0	-5.0^{-1}	6.6^{-3}	0.18	9.4^{-3}	-8.1^{-2}	8.9^{-3}	1.2^{-2}	8.3^{-3}
10	0.5	3	0.1	1.5^{-2}	9.0^{-3}	0.27	1.1^{-2}	1.5^{-2}	9.0^{-3}	1.9^{-2}	9.5^{-3}
10	0.5	3	1.0	-2.6^{-1}	9.4^{-3}	0.26	1.2^{-2}	-1.1^{-1}	1.0^{-2}	5.7^{-3}	1.0^{-2}
10	0.5	3	2.0	-7.5^{-1}	9.0^{-3}	0.26	1.2^{-2}	-1.3^{-1}	1.1^{-2}	8.0^{-3}	1.0^{-2}
20	0.1	1	0.1	9.0^{-4}	2.8^{-3}	0.02	2.9^{-3}	9.0^{-4}	2.8^{-3}	2.0^{-3}	2.8^{-3}
20	0.1	1	1.0	-8.8^{-2}	2.8^{-3}	0.02	2.9^{-3}	-1.3^{-2}	2.9^{-3}	-2.5^{-3}	2.9^{-3}
20	0.1	1	2.0	-2.4^{-1}	3.0^{-3}	0.02	3.1^{-3}	-4.3^{-3}	3.0^{-3}	6.0^{-3}	3.0^{-3}
20	0.1	2	0.1	-1.2^{-4}	4.5^{-3}	0.04	4.7^{-3}	-1.2^{-4}	4.5^{-3}	1.6^{-3}	4.5^{-3}

Table C.1 continued

1	0.1	1	0.1	2.9^{-2}	1.4^{-2}	0.54	2.6^{-2}	2.9^{-2}	1.4^{-2}	4.2^{-2}	1.8^{-2}
20	0.1	2	1.0	-1.7^{-1}	4.0^{-3}	0.04	4.1^{-3}	-2.0^{-2}	4.0^{-3}	4.3^{-4}	3.9^{-3}
20	0.1	2	2.0	-4.7^{-1}	5.1^{-3}	0.04	4.3^{-3}	-1.8^{-2}	4.2^{-3}	1.6^{-3}	4.2^{-3}
20	0.1	3	0.1	2.2^{-3}	5.8^{-3}	0.06	6.0^{-3}	2.2^{-3}	5.8^{-3}	4.1^{-3}	5.8^{-3}
20	0.1	3	1.0	-2.5^{-1}	5.4^{-3}	0.06	5.4^{-3}	-2.6^{-2}	5.3^{-3}	6.2^{-3}	5.3^{-3}
20	0.1	3	2.0	-7.2^{-1}	6.7^{-3}	0.06	5.3^{-3}	-2.9^{-2}	5.1^{-3}	1.9^{-3}	5.1^{-3}
20	0.2	1	0.1	-3.8^{-3}	3.3^{-3}	0.02	3.4^{-3}	-3.8^{-3}	3.3^{-3}	-2.9^{-3}	3.3^{-3}
20	0.2	1	1.0	-8.7^{-2}	3.1^{-3}	0.03	3.2^{-3}	-1.3^{-2}	3.1^{-3}	3.8^{-4}	3.1^{-3}
20	0.2	1	2.0	-2.4^{-1}	3.2^{-3}	0.03	3.6^{-3}	-6.2^{-3}	3.5^{-3}	6.4^{-3}	3.5^{-3}
20	0.2	2	0.1	5.5^{-3}	4.6^{-3}	0.06	4.9^{-3}	5.5^{-3}	4.6^{-3}	7.0^{-3}	4.7^{-3}
20	0.2	2	1.0	-1.6^{-1}	4.3^{-3}	0.06	4.7^{-3}	-1.5^{-2}	4.5^{-3}	1.1^{-2}	4.5^{-3}
20	0.2	2	2.0	-4.9^{-1}	4.9^{-3}	0.06	4.4^{-3}	-1.4^{-2}	4.2^{-3}	1.1^{-2}	4.2^{-3}
20	0.2	3	0.1	1.4^{-3}	5.4^{-3}	0.08	5.8^{-3}	1.4^{-3}	5.4^{-3}	3.3^{-3}	5.5^{-3}
20	0.2	3	1.0	-2.5^{-1}	4.9^{-3}	0.08	5.6^{-3}	-3.4^{-2}	5.3^{-3}	6.3^{-3}	5.3^{-3}
20	0.2	3	2.0	-7.5^{-1}	6.7^{-3}	0.08	6.0^{-3}	-2.9^{-2}	5.7^{-3}	8.2^{-3}	5.7^{-3}
20	0.5	1	0.1	-3.0^{-3}	4.0^{-3}	0.04	4.3^{-3}	-3.0^{-3}	4.0^{-3}	-1.1^{-3}	4.1^{-3}
20	0.5	1	1.0	-9.2^{-2}	4.1^{-3}	0.04	4.8^{-3}	-1.8^{-2}	4.5^{-3}	1.0^{-3}	4.6^{-3}
20	0.5	1	2.0	-2.5^{-1}	3.5^{-3}	0.04	4.5^{-3}	-2.0^{-2}	4.2^{-3}	-2.4^{-3}	4.3^{-3}
20	0.5	2	0.1	-6.3^{-3}	5.4^{-3}	0.07	6.0^{-3}	-6.2^{-3}	5.4^{-3}	-3.8^{-3}	5.6^{-3}
20	0.5	2	1.0	-1.8^{-1}	5.7^{-3}	0.08	6.3^{-3}	-3.4^{-2}	5.9^{-3}	3.0^{-3}	5.9^{-3}
20	0.5	2	2.0	-5.1^{-1}	5.0^{-3}	0.07	6.0^{-3}	-4.6^{-2}	5.6^{-3}	-9.3^{-3}	5.6^{-3}
20	0.5	3	0.1	8.1^{-4}	6.9^{-3}	0.12	7.7^{-3}	8.8^{-4}	6.9^{-3}	4.8^{-3}	7.2^{-3}
20	0.5	3	1.0	-2.7^{-1}	7.2^{-3}	0.12	8.1^{-3}	-4.9^{-2}	7.6^{-3}	7.1^{-3}	7.6^{-3}
20	0.5	3	2.0	-7.6^{-1}	6.7^{-3}	0.11	8.5^{-3}	-6.0^{-2}	7.9^{-3}	-5.3^{-3}	8.0^{-3}
80	0.1	1	0.1	-3.5^{-3}	1.5^{-3}	0.00	1.5^{-3}	-3.5^{-3}	1.5^{-3}	-2.7^{-3}	1.5^{-3}
80	0.1	1	1.0	-8.2^{-2}	1.7^{-3}	0.01	1.5^{-3}	1.1^{-3}	1.5^{-3}	-1.7^{-4}	2.6^{-3}
80	0.1	1	2.0	-2.4^{-1}	2.1^{-3}	0.00	1.3^{-3}	-2.7^{-3}	1.3^{-3}		
80	0.1	2	0.1	-2.2^{-3}	2.0^{-3}	0.01	2.0^{-3}	-2.2^{-3}	2.0^{-3}	-3.2^{-4}	2.0^{-3}
80	0.1	2	1.0	-1.7^{-1}	2.6^{-3}	0.01	2.0^{-3}	-3.8^{-3}	2.0^{-3}	-4.3^{-3}	3.4^{-3}
80	0.1	2	2.0	-4.8^{-1}	4.0^{-3}	0.01	2.1^{-3}	-6.7^{-3}	2.1^{-3}		
80	0.1	3	0.1	-2.8^{-3}	2.6^{-3}	0.01	2.6^{-3}	-2.8^{-3}	2.6^{-3}	6.4^{-5}	2.6^{-3}
80	0.1	3	1.0	-2.6^{-1}	3.7^{-3}	0.02	2.7^{-3}	-5.2^{-3}	2.6^{-3}	-7.0^{-3}	4.4^{-3}

Table C.1 continued

1	0.1	1	0.1	2.9^{-2}	1.4^{-2}	0.54	2.6^{-2}	2.9^{-2}	1.4^{-2}	4.2^{-2}	1.8^{-2}
80	0.1	3	2.0	-7.3^{-1}	5.9^{-3}	0.01	2.5^{-3}	-1.0^{-2}	2.5^{-3}		
80	0.2	1	0.1	-1.7^{-3}	1.6^{-3}	0.01	1.6^{-3}	-1.7^{-3}	1.6^{-3}	-8.3^{-4}	1.6^{-3}
80	0.2	1	1.0	-8.6^{-2}	1.8^{-3}	0.01	1.7^{-3}	-7.4^{-4}	1.7^{-3}	2.4^{-3}	1.7^{-3}
80	0.2	1	2.0	-2.5^{-1}	2.1^{-3}	0.01	1.6^{-3}	-9.0^{-5}	1.6^{-3}	-6.8^{-3}	5.1^{-3}
80	0.2	2	0.1	-1.1^{-3}	2.1^{-3}	0.01	2.1^{-3}	-1.1^{-3}	2.1^{-3}	8.8^{-4}	2.1^{-3}
80	0.2	2	1.0	-1.7^{-1}	2.8^{-3}	0.01	2.2^{-3}	-4.2^{-3}	2.2^{-3}	1.8^{-3}	2.2^{-3}
80	0.2	2	2.0	-5.0^{-1}	4.0^{-3}	0.02	2.1^{-3}	-2.1^{-3}	2.1^{-3}	-1.9^{-2}	6.9^{-3}
80	0.2	3	0.1	-1.3^{-3}	2.8^{-3}	0.02	2.8^{-3}	-1.3^{-3}	2.8^{-3}	1.6^{-3}	2.8^{-3}
80	0.2	3	1.0	-2.6^{-1}	3.9^{-3}	0.02	2.9^{-3}	-6.2^{-3}	2.9^{-3}	3.1^{-3}	2.9^{-3}
80	0.2	3	2.0	-7.5^{-1}	5.6^{-3}	0.02	2.9^{-3}	-4.8^{-3}	2.9^{-3}	-1.8^{-2}	9.8^{-3}
80	0.5	1	0.1	-7.5^{-4}	1.8^{-3}	0.01	1.9^{-3}	-7.5^{-4}	1.8^{-3}	2.9^{-4}	1.8^{-3}
80	0.5	1	1.0	-9.0^{-2}	2.1^{-3}	0.01	2.1^{-3}	-3.0^{-3}	2.1^{-3}	1.5^{-3}	2.1^{-3}
80	0.5	1	2.0	-2.5^{-1}	2.6^{-3}	0.01	2.0^{-3}	-2.3^{-3}	2.0^{-3}	1.8^{-3}	2.1^{-3}
80	0.5	2	0.1	-4.9^{-3}	2.8^{-3}	0.02	2.9^{-3}	-4.9^{-3}	2.8^{-3}	-2.6^{-3}	2.9^{-3}
80	0.5	2	1.0	-1.8^{-1}	3.2^{-3}	0.02	2.8^{-3}	-5.5^{-3}	2.8^{-3}	3.3^{-3}	2.8^{-3}
80	0.5	2	2.0	-5.0^{-1}	4.1^{-3}	0.02	2.6^{-3}	-1.0^{-2}	2.6^{-3}	-2.8^{-3}	2.6^{-3}
80	0.5	3	0.1	-8.5^{-3}	3.6^{-3}	0.02	3.7^{-3}	-8.5^{-3}	3.6^{-3}	-5.0^{-3}	3.6^{-3}
80	0.5	3	1.0	-2.8^{-1}	4.1^{-3}	0.03	3.7^{-3}	-1.3^{-2}	3.6^{-3}	2.2^{-5}	3.6^{-3}
80	0.5	3	2.0	-7.6^{-1}	5.8^{-3}	0.02	3.7^{-3}	-1.7^{-2}	3.6^{-3}	-5.5^{-3}	3.7^{-3}

TABLE C.2: 95% confidence interval coverage rates for simulations with $n = 100$. The model included three slope parameters (β_p). Simulations varied the number of cases (c), the ratio of cases to controls (r), and the magnitude of the variance of the individual-specific random effect (σ_α). Models used were the prospective logistic model (PLM), stratified case-control model (SCC), marginal logistic model (MLM), and the conditional logistic model (CLM). Empty cells indicate complete convergence failure for the given model and simulation parameter values. Superscripts indicate the exponents of scientific notation.

c	r	β_p	σ_α	PLM	SCC	MLM	CLM
1	0.1	1	1.0	0.89	0.47	0.89	0.95
1	0.1	1	2.0	0.59	0.45	0.65	0.95
1	0.1	2	0.1	0.95	0.14	0.95	0.95
1	0.1	2	1.0	0.84	0.14	0.84	0.94
1	0.1	2	2.0	0.25	0.10	0.33	0.98
1	0.1	3	0.1	0.97	0.04	0.97	0.97
1	0.1	3	1.0	0.81	0.06	0.81	0.97
1	0.1	3	2.0	0.10	0.04	0.21	0.98
1	0.2	1	0.1	0.95	0.52	0.95	0.97
1	0.2	1	1.0	0.94	0.48	0.94	0.96
1	0.2	1	2.0	0.59	0.56	0.59	0.92
1	0.2	2	0.1	0.96	0.12	0.96	0.98
1	0.2	2	1.0	0.88	0.14	0.88	0.95
1	0.2	2	2.0	0.31	0.17	0.33	0.96
1	0.2	3	0.1	0.95	0.06	0.95	0.97
1	0.2	3	1.0	0.84	0.01	0.84	0.99
1	0.2	3	2.0	0.18	0.05	0.21	0.96
1	0.5	1	0.1	0.93	0.58	0.93	0.96
1	0.5	1	1.0	0.91	0.60	0.91	0.97
1	0.5	1	2.0	0.76	0.65	0.76	0.96
1	0.5	2	0.1	0.96	0.30	0.96	0.97
1	0.5	2	1.0	0.93	0.20	0.93	0.98
1	0.5	2	2.0	0.48	0.23	0.48	0.98
1	0.5	3	0.1	0.94	0.07	0.94	0.96
1	0.5	3	1.0	0.89	0.03	0.89	0.98

Table C.2 continued

1	0.1	1	0.1	0.95	0.40	0.95	0.93
1	0.5	3	2.0	0.32	0.05	0.32	0.97
2	0.1	1	0.1	0.94	0.55	0.94	0.95
2	0.1	1	1.0	0.91	0.55	0.91	0.97
2	0.1	1	2.0	0.27	0.61	0.74	0.94
2	0.1	2	0.1	0.96	0.21	0.96	0.96
2	0.1	2	1.0	0.72	0.35	0.75	0.93
2	0.1	2	2.0	0.03	0.30	0.59	0.95
2	0.1	3	0.1	0.96	0.13	0.96	1.00
2	0.1	3	1.0	0.63	0.21	0.66	0.95
2	0.1	3	2.0	0.00	0.17	0.51	0.94
2	0.2	1	0.1	0.93	0.47	0.93	0.95
2	0.2	1	1.0	0.93	0.48	0.93	0.94
2	0.2	1	2.0	0.46	0.43	0.80	0.97
2	0.2	2	0.1	0.93	0.22	0.93	0.95
2	0.2	2	1.0	0.81	0.15	0.81	0.96
2	0.2	2	2.0	0.08	0.11	0.61	0.95
2	0.2	3	0.1	0.94	0.09	0.94	0.96
2	0.2	3	1.0	0.71	0.12	0.71	0.94
2	0.2	3	2.0	0.03	0.07	0.46	0.96
2	0.5	1	0.1	0.94	0.41	0.94	0.93
2	0.5	1	1.0	0.90	0.35	0.90	0.94
2	0.5	1	2.0	0.51	0.31	0.62	0.93
2	0.5	2	0.1	0.96	0.07	0.96	0.96
2	0.5	2	1.0	0.85	0.10	0.86	0.95
2	0.5	2	2.0	0.19	0.07	0.43	0.98
2	0.5	3	0.1	0.95	0.03	0.95	0.97
2	0.5	3	1.0	0.78	0.05	0.78	0.91
2	0.5	3	2.0	0.09	0.02	0.34	0.98
5	0.1	1	0.1	0.95	0.81	0.95	0.94
5	0.1	1	1.0	0.83	0.81	0.90	0.95
5	0.1	1	2.0	0.03	0.85	0.91	0.96

Table C.2 continued

1	0.1	1	0.1	0.95	0.40	0.95	0.93
5	0.1	2	0.1	0.96	0.65	0.96	0.95
5	0.1	2	1.0	0.55	0.59	0.79	0.93
5	0.1	2	2.0	0.00	0.64	0.83	0.95
5	0.1	3	0.1	0.96	0.49	0.96	0.95
5	0.1	3	1.0	0.39	0.52	0.77	0.91
5	0.1	3	2.0	0.00	0.55	0.82	0.97
5	0.2	1	0.1	0.92	0.74	0.92	0.93
5	0.2	1	1.0	0.79	0.70	0.89	0.97
5	0.2	1	2.0	0.07	0.72	0.87	0.96
5	0.2	2	0.1	0.92	0.56	0.92	0.96
5	0.2	2	1.0	0.63	0.54	0.78	0.95
5	0.2	2	2.0	0.00	0.62	0.79	0.95
5	0.2	3	0.1	0.96	0.39	0.96	0.94
5	0.2	3	1.0	0.49	0.43	0.73	0.95
5	0.2	3	2.0	0.00	0.49	0.71	0.93
5	0.5	1	0.1	0.96	0.57	0.96	0.94
5	0.5	1	1.0	0.85	0.59	0.91	0.94
5	0.5	1	2.0	0.13	0.61	0.83	0.97
5	0.5	2	0.1	0.97	0.33	0.97	0.94
5	0.5	2	1.0	0.67	0.40	0.79	0.93
5	0.5	2	2.0	0.00	0.38	0.80	0.96
5	0.5	3	0.1	0.95	0.21	0.95	0.97
5	0.5	3	1.0	0.55	0.19	0.75	0.93
5	0.5	3	2.0	0.00	0.23	0.75	0.98
10	0.1	1	0.1	0.96	0.87	0.96	0.94
10	0.1	1	1.0	0.57	0.88	0.91	0.93
10	0.1	1	2.0	0.01	0.85	0.91	0.91
10	0.1	2	0.1	0.99	0.83	0.99	0.99
10	0.1	2	1.0	0.27	0.79	0.89	0.94
10	0.1	2	2.0	0.00	0.79	0.93	0.98
10	0.1	3	0.1	0.97	0.79	0.97	0.96

Table C.2 continued

1	0.1	1	0.1	0.95	0.40	0.95	0.93
10	0.1	3	1.0	0.15	0.78	0.83	0.95
10	0.1	3	2.0	0.00	0.77	0.91	0.95
10	0.2	1	0.1	0.96	0.84	0.96	0.93
10	0.2	1	1.0	0.67	0.88	0.93	0.94
10	0.2	1	2.0	0.00	0.83	0.91	0.92
10	0.2	2	0.1	0.93	0.73	0.93	0.94
10	0.2	2	1.0	0.33	0.79	0.93	0.98
10	0.2	2	2.0	0.00	0.76	0.91	0.97
10	0.2	3	0.1	0.93	0.69	0.93	0.93
10	0.2	3	1.0	0.17	0.69	0.89	0.97
10	0.2	3	2.0	0.00	0.73	0.91	0.95
10	0.5	1	0.1	0.95	0.83	0.95	0.95
10	0.5	1	1.0	0.67	0.85	0.91	0.95
10	0.5	1	2.0	0.03	0.77	0.93	0.97
10	0.5	2	0.1	0.97	0.65	0.97	0.97
10	0.5	2	1.0	0.53	0.64	0.93	0.96
10	0.5	2	2.0	0.00	0.62	0.89	0.94
10	0.5	3	0.1	0.97	0.49	0.97	0.96
10	0.5	3	1.0	0.33	0.58	0.88	0.95
10	0.5	3	2.0	0.00	0.54	0.83	0.95
20	0.1	1	0.1	0.97	0.92	0.97	0.97
20	0.1	1	1.0	0.28	0.91	0.95	0.94
20	0.1	1	2.0	0.00	0.89	0.95	0.93
20	0.1	2	0.1	0.89	0.86	0.89	0.89
20	0.1	2	1.0	0.05	0.89	0.91	0.95
20	0.1	2	2.0	0.00	0.87	0.93	0.95
20	0.1	3	0.1	0.91	0.85	0.91	0.91
20	0.1	3	1.0	0.01	0.84	0.90	0.93
20	0.1	3	2.0	0.00	0.86	0.91	0.95
20	0.2	1	0.1	0.96	0.95	0.96	0.97
20	0.2	1	1.0	0.40	0.94	0.95	0.97

Table C.2 continued

1	0.1	1	0.1	0.95	0.40	0.95	0.93
20	0.2	1	2.0	0.00	0.85	0.97	0.97
20	0.2	2	0.1	0.93	0.83	0.93	0.94
20	0.2	2	1.0	0.13	0.81	0.95	0.97
20	0.2	2	2.0	0.00	0.85	0.95	0.97
20	0.2	3	0.1	0.97	0.84	0.97	0.97
20	0.2	3	1.0	0.01	0.83	0.96	0.97
20	0.2	3	2.0	0.00	0.82	0.93	0.94
20	0.5	1	0.1	0.95	0.87	0.95	0.95
20	0.5	1	1.0	0.51	0.83	0.91	0.91
20	0.5	1	2.0	0.00	0.89	0.91	0.94
20	0.5	2	0.1	0.96	0.84	0.96	0.95
20	0.5	2	1.0	0.21	0.76	0.93	0.95
20	0.5	2	2.0	0.00	0.83	0.89	0.93
20	0.5	3	0.1	0.96	0.77	0.96	0.97
20	0.5	3	1.0	0.11	0.72	0.89	0.95
20	0.5	3	2.0	0.00	0.75	0.89	0.90
80	0.1	1	0.1	0.97	0.97	0.97	0.98
80	0.1	1	1.0	0.02	0.92	0.96	0.96
80	0.1	1	2.0	0.00	0.99	0.98	
80	0.1	2	0.1	0.95	0.95	0.95	0.95
80	0.1	2	1.0	0.00	0.93	0.95	0.96
80	0.1	2	2.0	0.00	0.93	0.94	
80	0.1	3	0.1	0.93	0.92	0.93	0.93
80	0.1	3	1.0	0.00	0.93	0.93	0.92
80	0.1	3	2.0	0.00	0.95	0.93	
80	0.2	1	0.1	0.97	0.95	0.97	0.99
80	0.2	1	1.0	0.00	0.92	0.93	0.94
80	0.2	1	2.0	0.00	0.96	0.96	1.00
80	0.2	2	0.1	0.95	0.96	0.95	0.95
80	0.2	2	1.0	0.00	0.96	0.95	0.95
80	0.2	2	2.0	0.00	0.93	0.98	1.00

Table C.2 continued

1	0.1	1	0.1	0.95	0.40	0.95	0.93
80	0.2	3	0.1	0.95	0.93	0.95	0.96
80	0.2	3	1.0	0.00	0.91	0.96	0.97
80	0.2	3	2.0	0.00	0.93	0.94	1.00
80	0.5	1	0.1	0.97	0.95	0.97	0.97
80	0.5	1	1.0	0.05	0.92	0.95	0.94
80	0.5	1	2.0	0.00	0.93	0.95	0.95
80	0.5	2	0.1	0.97	0.90	0.97	0.95
80	0.5	2	1.0	0.00	0.90	0.93	0.93
80	0.5	2	2.0	0.00	0.93	0.95	0.97
80	0.5	3	0.1	0.94	0.93	0.94	0.97
80	0.5	3	1.0	0.00	0.89	0.94	0.96
80	0.5	3	2.0	0.00	0.93	0.93	0.95

SIMULATION RESULTS FOR $n = 30$

TABLE C.3: Estimated bias and Monte Carlo standard errors estimated from simulations with $n = 30$. The model included three slope parameters (β_p). Simulations varied the number of cases (c), the ratio of cases to controls (r), and the magnitude of the variance of the individual-specific random effect (σ_α). Methods used were the prospective logistic model (PLM), stratified case-control model (SCC), marginal logistic model (MLM), and the conditional logistic model (CLM). Superscripts indicate the exponents of scientific notation.

c	r	β_p	σ_α	PLM	SE	SCC	SE	MLM	SE	CLM	SE
1	0.1	1	1.0	-3.8^{-2}	2.5^{-2}	0.42	4.4^{-2}	-3.6^{-2}	2.5^{-2}	1.0^{-1}	4.0^{-2}
1	0.1	1	2.0	-1.8^{-1}	2.4^{-2}	0.52	4.7^{-2}	-1.6^{-1}	2.5^{-2}	1.8^{-1}	4.2^{-2}
1	0.1	2	0.1	1.7^{-1}	3.5^{-2}	1.12	6.3^{-2}	1.8^{-1}	3.7^{-2}	4.4^{-1}	7.5^{-2}
1	0.1	2	1.0	-5.4^{-2}	3.6^{-2}	1.00	6.2^{-2}	-5.0^{-2}	3.6^{-2}	3.5^{-1}	6.5^{-2}
1	0.1	2	2.0	-3.6^{-1}	3.0^{-2}	1.00	6.1^{-2}	-3.2^{-1}	3.3^{-2}	3.5^{-1}	6.9^{-2}
1	0.1	3	0.1	2.6^{-1}	4.5^{-2}	1.69	8.4^{-2}	2.6^{-1}	4.6^{-2}	7.1^{-1}	1.1^{-1}
1	0.1	3	1.0	-7.3^{-2}	4.6^{-2}	1.48	8.6^{-2}	-6.6^{-2}	4.7^{-2}	4.8^{-1}	8.7^{-2}
1	0.1	3	2.0	-5.7^{-1}	3.5^{-2}	1.44	8.3^{-2}	-5.1^{-1}	4.2^{-2}	5.1^{-1}	9.8^{-2}
1	0.2	1	0.1	7.8^{-2}	3.5^{-2}	0.71	7.2^{-2}	7.9^{-2}	3.5^{-2}	5.8^{-1}	1.6^{-1}
1	0.2	1	1.0	1.3^{-2}	3.2^{-2}	0.60	6.4^{-2}	1.8^{-2}	3.3^{-2}	2.6^{-1}	7.9^{-2}
1	0.2	1	2.0	-1.8^{-1}	2.4^{-2}	0.71	6.5^{-2}	-1.7^{-1}	2.4^{-2}	2.5^{-1}	5.3^{-2}
1	0.2	2	0.1	1.9^{-1}	4.7^{-2}	1.26	9.3^{-2}	2.0^{-1}	4.8^{-2}	2.1^{0}	9.8^{-1}
1	0.2	2	1.0	-3.3^{-2}	4.0^{-2}	1.14	8.2^{-2}	-2.4^{-2}	4.2^{-2}	5.2^{-1}	1.4^{-1}
1	0.2	2	2.0	-3.5^{-1}	2.9^{-2}	1.32	7.8^{-2}	-3.3^{-1}	3.0^{-2}	5.4^{-1}	9.1^{-2}
1	0.2	3	0.1	2.7^{-1}	5.7^{-2}	1.97	1.1^{-1}	2.8^{-1}	5.8^{-2}	2.6^{0}	1.1^{0}
1	0.2	3	1.0	-9.4^{-3}	5.1^{-2}	1.87	1.0^{-1}	5.5^{-3}	5.6^{-2}	7.7^{-1}	1.8^{-1}
1	0.2	3	2.0	-5.0^{-1}	3.8^{-2}	2.01	1.2^{-1}	-4.4^{-1}	4.2^{-2}	9.6^{-1}	1.6^{-1}
1	0.5	1	0.1	1.9^{-1}	4.3^{-2}	1.00	1.5^{-1}	2.8^{-1}	1.1^{-1}	1.4^{0}	8.2^{-1}
1	0.5	1	1.0	1.1^{-1}	4.9^{-2}	0.73	1.1^{-1}	2.5^{-1}	1.3^{-1}	5.3^{-1}	1.7^{-1}
1	0.5	1	2.0	-8.1^{-2}	3.8^{-2}	0.61	1.2^{-1}	5.0^{-1}	3.3^{-1}	2.6^{-1}	1.4^{-1}
1	0.5	2	0.1	3.6^{-1}	6.5^{-2}	1.62	1.6^{-1}	4.5^{-1}	1.3^{-1}	2.1^{0}	1.2^{0}
1	0.5	2	1.0	1.7^{-1}	5.9^{-2}	1.66	1.5^{-1}	4.0^{-1}	2.2^{-1}	1.0^{0}	2.2^{-1}
1	0.5	2	2.0	-1.8^{-1}	5.8^{-2}	1.32	1.4^{-1}	9.5^{-1}	5.8^{-1}	8.7^{-1}	2.5^{-1}
1	0.5	3	0.1	5.1^{-1}	9.1^{-2}	2.56	2.3^{-1}	6.5^{-1}	1.9^{-1}	2.8^{0}	1.5^{0}

Table C.3 continued

1	0.1	1	0.1	1.0^{-1}	2.8^{-2}	0.57	4.7^{-2}	1.1^{-1}	2.9^{-2}	3.0^{-1}	5.5^{-2}
1	0.5	3	1.0	2.7^{-1}	8.2^{-2}	2.34	1.7^{-1}	6.2^{-1}	3.4^{-1}	1.4^{0}	3.2^{-1}
1	0.5	3	2.0	-2.9^{-1}	7.0^{-2}	2.32	1.9^{-1}	1.5^{0}	1.0^{0}	1.4^{0}	3.2^{-1}
2	0.1	1	0.1	3.7^{-2}	1.7^{-2}	0.30	2.5^{-2}	3.7^{-2}	1.7^{-2}	3.9^{-2}	1.9^{-2}
2	0.1	1	1.0	-3.3^{-2}	1.8^{-2}	0.32	2.7^{-2}	-2.1^{-2}	1.9^{-2}	5.9^{-2}	2.3^{-2}
2	0.1	1	2.0	-2.1^{-1}	1.4^{-2}	0.32	2.8^{-2}	-9.8^{-2}	1.7^{-2}	5.6^{-2}	2.1^{-2}
2	0.1	2	0.1	5.5^{-2}	2.6^{-2}	0.58	4.0^{-2}	5.5^{-2}	2.6^{-2}	7.0^{-2}	2.9^{-2}
2	0.1	2	1.0	-8.8^{-2}	2.4^{-2}	0.60	4.0^{-2}	-5.9^{-2}	2.6^{-2}	9.6^{-2}	3.4^{-2}
2	0.1	2	2.0	-4.1^{-1}	2.0^{-2}	0.63	4.3^{-2}	-1.9^{-1}	2.8^{-2}	1.1^{-1}	3.3^{-2}
2	0.1	3	0.1	9.3^{-2}	3.3^{-2}	0.88	5.1^{-2}	9.3^{-2}	3.3^{-2}	1.2^{-1}	3.7^{-2}
2	0.1	3	1.0	-1.2^{-1}	3.0^{-2}	0.96	5.6^{-2}	-7.3^{-2}	3.4^{-2}	1.8^{-1}	4.4^{-2}
2	0.1	3	2.0	-6.4^{-1}	2.6^{-2}	0.93	6.1^{-2}	-3.0^{-1}	3.8^{-2}	1.5^{-1}	4.4^{-2}
2	0.2	1	0.1	3.2^{-2}	2.0^{-2}	0.44	3.4^{-2}	3.2^{-2}	2.0^{-2}	6.5^{-2}	2.3^{-2}
2	0.2	1	1.0	-5.9^{-2}	1.7^{-2}	0.40	3.0^{-2}	-4.2^{-2}	1.8^{-2}	5.6^{-2}	2.4^{-2}
2	0.2	1	2.0	-2.2^{-1}	1.8^{-2}	0.39	3.4^{-2}	-1.2^{-1}	2.0^{-2}	6.8^{-2}	2.6^{-2}
2	0.2	2	0.1	2.7^{-2}	2.6^{-2}	0.80	4.9^{-2}	2.7^{-2}	2.6^{-2}	7.5^{-2}	3.3^{-2}
2	0.2	2	1.0	-1.0^{-1}	2.4^{-2}	0.88	5.3^{-2}	-7.3^{-2}	2.5^{-2}	1.6^{-1}	3.6^{-2}
2	0.2	2	2.0	-4.3^{-1}	2.7^{-2}	0.81	5.4^{-2}	-2.3^{-1}	3.3^{-2}	1.7^{-1}	4.5^{-2}
2	0.2	3	0.1	7.9^{-2}	3.6^{-2}	1.29	7.2^{-2}	7.9^{-2}	3.6^{-2}	1.7^{-1}	4.6^{-2}
2	0.2	3	1.0	-1.4^{-1}	3.4^{-2}	1.32	7.6^{-2}	-8.7^{-2}	3.8^{-2}	2.4^{-1}	5.4^{-2}
2	0.2	3	2.0	-6.6^{-1}	3.2^{-2}	1.18	7.0^{-2}	-3.8^{-1}	4.2^{-2}	2.4^{-1}	6.0^{-2}
2	0.5	1	0.1	9.2^{-2}	2.3^{-2}	0.68	4.8^{-2}	9.6^{-2}	2.4^{-2}	2.7^{-1}	5.6^{-2}
2	0.5	1	1.0	-1.8^{-2}	2.7^{-2}	0.70	5.1^{-2}	4.4^{-3}	2.9^{-2}	2.3^{-1}	5.8^{-2}
2	0.5	1	2.0	-1.8^{-1}	2.1^{-2}	0.64	6.0^{-2}	-9.1^{-2}	3.5^{-2}	2.3^{-1}	6.1^{-2}
2	0.5	2	0.1	1.7^{-1}	3.7^{-2}	1.29	7.3^{-2}	1.8^{-1}	3.8^{-2}	4.8^{-1}	9.3^{-2}
2	0.5	2	1.0	-1.1^{-1}	3.1^{-2}	1.25	7.2^{-2}	-6.1^{-2}	3.9^{-2}	3.2^{-1}	9.4^{-2}
2	0.5	2	2.0	-3.7^{-1}	2.3^{-2}	1.30	7.2^{-2}	-2.0^{-1}	6.3^{-2}	4.1^{-1}	7.3^{-2}
2	0.5	3	0.1	2.6^{-1}	4.9^{-2}	1.95	8.9^{-2}	2.8^{-1}	5.1^{-2}	7.5^{-1}	1.4^{-1}
2	0.5	3	1.0	-9.4^{-2}	4.6^{-2}	1.98	1.0^{-1}	-2.3^{-2}	5.8^{-2}	5.5^{-1}	1.5^{-1}
2	0.5	3	2.0	-5.9^{-1}	3.0^{-2}	1.94	1.0^{-1}	-3.1^{-1}	9.6^{-2}	6.3^{-1}	1.2^{-1}
5	0.1	1	0.1	1.7^{-2}	1.1^{-2}	0.10	1.2^{-2}	1.7^{-2}	1.1^{-2}	1.4^{-2}	1.1^{-2}
5	0.1	1	1.0	-4.8^{-2}	1.1^{-2}	0.12	1.2^{-2}	-6.8^{-3}	1.1^{-2}	4.0^{-2}	1.1^{-2}

Table C.3 continued

1	0.1	1	0.1	1.0^{-1}	2.8^{-2}	0.57	4.7^{-2}	1.1^{-1}	2.9^{-2}	3.0^{-1}	5.5^{-2}
5	0.1	1	2.0	-2.4^{-1}	9.5^{-3}	0.07	1.3^{-2}	-5.5^{-2}	1.1^{-2}	-7.3^{-3}	1.2^{-2}
5	0.1	2	0.1	3.6^{-2}	1.5^{-2}	0.20	1.7^{-2}	3.6^{-2}	1.5^{-2}	3.1^{-2}	1.5^{-2}
5	0.1	2	1.0	-1.5^{-1}	1.3^{-2}	0.19	1.6^{-2}	-6.6^{-2}	1.4^{-2}	2.2^{-2}	1.4^{-2}
5	0.1	2	2.0	-4.6^{-1}	1.3^{-2}	0.18	1.7^{-2}	-7.8^{-2}	1.5^{-2}	1.8^{-2}	1.5^{-2}
5	0.1	3	0.1	5.5^{-2}	2.0^{-2}	0.29	2.3^{-2}	5.5^{-2}	2.0^{-2}	4.6^{-2}	2.0^{-2}
5	0.1	3	1.0	-2.1^{-1}	1.7^{-2}	0.30	2.1^{-2}	-8.4^{-2}	1.8^{-2}	5.1^{-2}	1.8^{-2}
5	0.1	3	2.0	-7.0^{-1}	1.7^{-2}	0.25	2.3^{-2}	-1.3^{-1}	2.0^{-2}	6.6^{-3}	2.0^{-2}
5	0.2	1	0.1	-3.6^{-3}	1.3^{-2}	0.12	1.6^{-2}	-2.6^{-3}	1.3^{-2}	8.8^{-5}	1.4^{-2}
5	0.2	1	1.0	-6.6^{-2}	1.1^{-2}	0.14	1.4^{-2}	-3.2^{-2}	1.2^{-2}	2.9^{-2}	1.2^{-2}
5	0.2	1	2.0	-2.2^{-1}	1.1^{-2}	0.16	1.6^{-2}	-2.2^{-2}	1.3^{-2}	4.0^{-2}	1.4^{-2}
5	0.2	2	0.1	4.6^{-2}	1.8^{-2}	0.29	2.5^{-2}	4.8^{-2}	1.8^{-2}	5.2^{-2}	2.1^{-2}
5	0.2	2	1.0	-1.7^{-1}	1.4^{-2}	0.24	2.0^{-2}	-1.0^{-1}	1.6^{-2}	7.3^{-3}	1.7^{-2}
5	0.2	2	2.0	-4.6^{-1}	1.5^{-2}	0.29	2.4^{-2}	-7.6^{-2}	1.9^{-2}	4.7^{-2}	2.0^{-2}
5	0.2	3	0.1	4.6^{-2}	2.2^{-2}	0.42	3.0^{-2}	4.9^{-2}	2.2^{-2}	6.2^{-2}	2.4^{-2}
5	0.2	3	1.0	-2.4^{-1}	1.9^{-2}	0.37	2.8^{-2}	-1.5^{-1}	2.2^{-2}	2.1^{-2}	2.3^{-2}
5	0.2	3	2.0	-7.1^{-1}	1.8^{-2}	0.42	3.2^{-2}	-1.3^{-1}	2.5^{-2}	6.5^{-2}	2.6^{-2}
5	0.5	1	0.1	2.9^{-2}	1.6^{-2}	0.24	2.5^{-2}	3.2^{-2}	1.7^{-2}	3.4^{-2}	1.9^{-2}
5	0.5	1	1.0	-7.0^{-2}	1.5^{-2}	0.22	2.2^{-2}	-4.8^{-2}	1.5^{-2}	2.1^{-2}	1.7^{-2}
5	0.5	1	2.0	-2.3^{-1}	1.2^{-2}	0.22	2.0^{-2}	-7.1^{-2}	1.5^{-2}	1.7^{-2}	1.6^{-2}
5	0.5	2	0.1	1.4^{-2}	2.0^{-2}	0.42	3.5^{-2}	1.9^{-2}	2.1^{-2}	2.5^{-2}	2.5^{-2}
5	0.5	2	1.0	-9.9^{-2}	2.2^{-2}	0.49	3.5^{-2}	-5.5^{-2}	2.3^{-2}	7.6^{-2}	2.6^{-2}
5	0.5	2	2.0	-4.5^{-1}	1.8^{-2}	0.48	3.7^{-2}	-1.1^{-1}	2.5^{-2}	6.6^{-2}	2.7^{-2}
5	0.5	3	0.1	5.1^{-2}	2.8^{-2}	0.67	4.8^{-2}	5.9^{-2}	2.9^{-2}	6.8^{-2}	3.4^{-2}
5	0.5	3	1.0	-1.7^{-1}	2.5^{-2}	0.71	4.5^{-2}	-1.0^{-1}	2.7^{-2}	9.8^{-2}	3.2^{-2}
5	0.5	3	2.0	-6.8^{-1}	2.2^{-2}	0.73	5.1^{-2}	-1.7^{-1}	3.5^{-2}	1.0^{-1}	3.6^{-2}
10	0.1	1	0.1	1.6^{-2}	8.1^{-3}	0.05	8.4^{-3}	1.6^{-2}	8.1^{-3}	1.5^{-2}	8.0^{-3}
10	0.1	1	1.0	-8.3^{-2}	7.4^{-3}	0.04	7.8^{-3}	-2.3^{-2}	7.3^{-3}	-1.2^{-3}	7.5^{-3}
10	0.1	1	2.0	-2.4^{-1}	8.0^{-3}	0.04	8.3^{-3}	-2.2^{-2}	7.9^{-3}	-2.9^{-4}	7.9^{-3}
10	0.1	2	0.1	2.3^{-3}	1.1^{-2}	0.08	1.1^{-2}	2.4^{-3}	1.1^{-2}	2.8^{-3}	1.1^{-2}
10	0.1	2	1.0	-1.5^{-1}	1.0^{-2}	0.09	1.1^{-2}	-3.0^{-2}	9.9^{-3}	1.2^{-2}	1.0^{-2}
10	0.1	2	2.0	-4.5^{-1}	1.0^{-2}	0.10	1.2^{-2}	-2.2^{-2}	1.1^{-2}	2.2^{-2}	1.1^{-2}

Table C.3 continued

1	0.1	1	0.1	1.0^{-1}	2.8^{-2}	0.57	4.7^{-2}	1.1^{-1}	2.9^{-2}	3.0^{-1}	5.5^{-2}
10	0.1	3	0.1	-4.8^{-3}	1.3^{-2}	0.11	1.4^{-2}	-4.8^{-3}	1.3^{-2}	-4.1^{-3}	1.3^{-2}
10	0.1	3	1.0	-2.4^{-1}	1.3^{-2}	0.12	1.3^{-2}	-6.0^{-2}	1.2^{-2}	7.7^{-3}	1.2^{-2}
10	0.1	3	2.0	-6.9^{-1}	1.5^{-2}	0.15	1.5^{-2}	-3.5^{-2}	1.4^{-2}	3.1^{-2}	1.4^{-2}
10	0.2	1	0.1	1.2^{-2}	9.2^{-3}	0.07	9.8^{-3}	1.2^{-2}	9.2^{-3}	1.4^{-2}	9.2^{-3}
10	0.2	1	1.0	-7.1^{-2}	8.5^{-3}	0.08	9.9^{-3}	-8.7^{-3}	9.1^{-3}	2.2^{-2}	9.2^{-3}
10	0.2	1	2.0	-2.3^{-1}	8.6^{-3}	0.07	9.5^{-3}	-1.4^{-2}	9.0^{-3}	1.4^{-2}	8.9^{-3}
10	0.2	2	0.1	2.3^{-2}	1.3^{-2}	0.13	1.4^{-2}	2.3^{-2}	1.3^{-2}	2.4^{-2}	1.3^{-2}
10	0.2	2	1.0	-1.5^{-1}	1.2^{-2}	0.13	1.4^{-2}	-3.1^{-2}	1.3^{-2}	2.4^{-2}	1.3^{-2}
10	0.2	2	2.0	-4.7^{-1}	1.1^{-2}	0.12	1.2^{-2}	-4.4^{-2}	1.1^{-2}	1.2^{-2}	1.1^{-2}
10	0.2	3	0.1	1.9^{-2}	1.6^{-2}	0.18	1.7^{-2}	1.9^{-2}	1.6^{-2}	2.0^{-2}	1.6^{-2}
10	0.2	3	1.0	-2.2^{-1}	1.5^{-2}	0.20	1.8^{-2}	-3.9^{-2}	1.6^{-2}	4.4^{-2}	1.6^{-2}
10	0.2	3	2.0	-7.1^{-1}	1.5^{-2}	0.18	1.6^{-2}	-6.0^{-2}	1.5^{-2}	2.5^{-2}	1.4^{-2}
10	0.5	1	0.1	2.2^{-2}	1.1^{-2}	0.11	1.2^{-2}	2.2^{-2}	1.1^{-2}	2.0^{-2}	1.1^{-2}
10	0.5	1	1.0	-8.5^{-2}	9.9^{-3}	0.09	1.2^{-2}	-3.4^{-2}	1.0^{-2}	2.5^{-3}	1.1^{-2}
10	0.5	1	2.0	-2.4^{-1}	9.9^{-3}	0.09	1.3^{-2}	-4.5^{-2}	1.2^{-2}	1.4^{-3}	1.1^{-2}
10	0.5	2	0.1	3.4^{-2}	1.5^{-2}	0.21	1.8^{-2}	3.4^{-2}	1.5^{-2}	3.7^{-2}	1.6^{-2}
10	0.5	2	1.0	-1.5^{-1}	1.4^{-2}	0.22	1.9^{-2}	-3.9^{-2}	1.6^{-2}	4.4^{-2}	1.6^{-2}
10	0.5	2	2.0	-4.7^{-1}	1.3^{-2}	0.17	1.8^{-2}	-8.4^{-2}	1.6^{-2}	7.3^{-3}	1.6^{-2}
10	0.5	3	0.1	5.1^{-2}	2.1^{-2}	0.31	2.4^{-2}	5.1^{-2}	2.1^{-2}	5.3^{-2}	2.1^{-2}
10	0.5	3	1.0	-2.2^{-1}	1.8^{-2}	0.32	2.5^{-2}	-5.3^{-2}	2.1^{-2}	6.3^{-2}	2.2^{-2}
10	0.5	3	2.0	-7.2^{-1}	1.7^{-2}	0.25	2.3^{-2}	-1.4^{-1}	2.1^{-2}	3.1^{-3}	2.0^{-2}
20	0.1	1	0.1	1.4^{-2}	5.8^{-3}	0.03	5.9^{-3}	1.4^{-2}	5.8^{-3}	1.4^{-2}	5.8^{-3}
20	0.1	1	1.0	-7.5^{-2}	5.6^{-3}	0.03	5.8^{-3}	-1.9^{-3}	5.6^{-3}	8.6^{-3}	5.6^{-3}
20	0.1	1	2.0	-2.3^{-1}	5.2^{-3}	0.02	5.0^{-3}	-1.0^{-2}	4.8^{-3}	-1.8^{-4}	4.9^{-3}
20	0.1	2	0.1	2.9^{-3}	7.7^{-3}	0.04	8.1^{-3}	3.0^{-3}	7.7^{-3}	3.4^{-3}	7.9^{-3}
20	0.1	2	1.0	-1.6^{-1}	7.2^{-3}	0.05	7.3^{-3}	-1.2^{-2}	7.0^{-3}	9.0^{-3}	7.1^{-3}
20	0.1	2	2.0	-4.6^{-1}	8.7^{-3}	0.04	7.8^{-3}	-1.7^{-2}	7.6^{-3}	3.5^{-3}	7.6^{-3}
20	0.1	3	0.1	1.5^{-2}	9.7^{-3}	0.07	1.0^{-2}	1.5^{-2}	9.7^{-3}	1.5^{-2}	9.8^{-3}
20	0.1	3	1.0	-2.4^{-1}	9.5^{-3}	0.06	9.4^{-3}	-2.4^{-2}	9.0^{-3}	9.0^{-3}	9.0^{-3}
20	0.1	3	2.0	-7.1^{-1}	1.2^{-2}	0.06	8.7^{-3}	-2.8^{-2}	8.4^{-3}	3.1^{-3}	8.4^{-3}
20	0.2	1	0.1	8.4^{-3}	5.7^{-3}	0.03	5.8^{-3}	8.4^{-3}	5.7^{-3}	7.2^{-3}	5.6^{-3}

Table C.3 continued

1	0.1	1	0.1	1.0^{-1}	2.8^{-2}	0.57	4.7^{-2}	1.1^{-1}	2.9^{-2}	3.0^{-1}	5.5^{-2}
20	0.2	1	1.0	-8.8^{-2}	6.5^{-3}	0.03	6.6^{-3}	-1.3^{-2}	6.4^{-3}	2.4^{-4}	6.4^{-3}
20	0.2	1	2.0	-2.4^{-1}	6.0^{-3}	0.03	6.1^{-3}	-4.9^{-3}	5.8^{-3}	7.8^{-3}	5.9^{-3}
20	0.2	2	0.1	1.2^{-2}	7.2^{-3}	0.06	7.7^{-3}	1.3^{-2}	7.2^{-3}	1.3^{-2}	7.4^{-3}
20	0.2	2	1.0	-1.7^{-1}	7.7^{-3}	0.06	8.0^{-3}	-1.8^{-2}	7.6^{-3}	7.9^{-3}	7.6^{-3}
20	0.2	2	2.0	-4.8^{-1}	9.2^{-3}	0.05	8.5^{-3}	-2.0^{-2}	8.2^{-3}	4.5^{-3}	8.2^{-3}
20	0.2	3	0.1	1.5^{-2}	9.9^{-3}	0.09	1.0^{-2}	1.5^{-2}	9.9^{-3}	1.6^{-2}	9.9^{-3}
20	0.2	3	1.0	-2.6^{-1}	1.0^{-2}	0.08	1.1^{-2}	-3.2^{-2}	1.0^{-2}	7.8^{-3}	1.0^{-2}
20	0.2	3	2.0	-7.3^{-1}	1.3^{-2}	0.08	1.1^{-2}	-3.2^{-2}	1.0^{-2}	6.0^{-3}	1.0^{-2}
20	0.5	1	0.1	1.7^{-3}	7.9^{-3}	0.04	8.4^{-3}	1.7^{-3}	7.9^{-3}	8.6^{-4}	8.0^{-3}
20	0.5	1	1.0	-8.8^{-2}	6.8^{-3}	0.04	7.7^{-3}	-1.4^{-2}	7.3^{-3}	4.4^{-3}	7.3^{-3}
20	0.5	1	2.0	-2.5^{-1}	6.5^{-3}	0.05	8.4^{-3}	-1.2^{-2}	8.0^{-3}	7.5^{-3}	8.0^{-3}
20	0.5	2	0.1	4.6^{-3}	9.4^{-3}	0.08	1.0^{-2}	4.6^{-3}	9.4^{-3}	2.6^{-3}	9.4^{-3}
20	0.5	2	1.0	-1.6^{-1}	9.6^{-3}	0.10	1.2^{-2}	-1.5^{-2}	1.1^{-2}	2.1^{-2}	1.1^{-2}
20	0.5	2	2.0	-4.9^{-1}	9.0^{-3}	0.09	1.1^{-2}	-2.5^{-2}	1.0^{-2}	1.1^{-2}	1.0^{-2}
20	0.5	3	0.1	1.1^{-2}	1.4^{-2}	0.13	1.6^{-2}	1.1^{-2}	1.4^{-2}	8.8^{-3}	1.4^{-2}
20	0.5	3	1.0	-2.4^{-1}	1.3^{-2}	0.16	1.6^{-2}	-1.4^{-2}	1.4^{-2}	4.0^{-2}	1.4^{-2}
20	0.5	3	2.0	-7.4^{-1}	1.3^{-2}	0.13	1.4^{-2}	-4.8^{-2}	1.3^{-2}	7.3^{-3}	1.3^{-2}
80	0.1	1	0.1	4.3^{-3}	2.6^{-3}	0.01	2.6^{-3}	4.3^{-3}	2.6^{-3}	5.1^{-3}	2.6^{-3}
80	0.1	1	1.0	-8.2^{-2}	2.8^{-3}	0.00	2.6^{-3}	-5.5^{-3}	2.5^{-3}	-6.3^{-3}	3.2^{-3}
80	0.1	1	2.0	-2.4^{-1}	4.1^{-3}	0.00	2.3^{-3}	-2.3^{-3}	2.3^{-3}	-1.8^{-2}	1.1^{-2}
80	0.1	2	0.1	2.7^{-3}	3.1^{-3}	0.01	3.1^{-3}	2.8^{-3}	3.1^{-3}	4.3^{-3}	3.1^{-3}
80	0.1	2	1.0	-1.6^{-1}	4.3^{-3}	0.01	3.7^{-3}	-7.1^{-3}	3.7^{-3}	-9.5^{-3}	4.2^{-3}
80	0.1	2	2.0	-4.8^{-1}	7.3^{-3}	0.01	3.9^{-3}	-4.4^{-3}	3.9^{-3}	-5.3^{-2}	2.5^{-2}
80	0.1	3	0.1	2.1^{-3}	4.2^{-3}	0.02	4.2^{-3}	2.2^{-3}	4.2^{-3}	4.6^{-3}	4.2^{-3}
80	0.1	3	1.0	-2.4^{-1}	6.2^{-3}	0.01	4.7^{-3}	-8.5^{-3}	4.7^{-3}	-1.2^{-2}	5.3^{-3}
80	0.1	3	2.0	-7.2^{-1}	1.0^{-2}	0.02	4.6^{-3}	-4.6^{-3}	4.5^{-3}	-8.4^{-2}	2.1^{-2}
80	0.2	1	0.1	-3.1^{-3}	3.0^{-3}	0.00	3.1^{-3}	-3.1^{-3}	3.0^{-3}	-2.4^{-3}	3.1^{-3}
80	0.2	1	1.0	-8.4^{-2}	3.6^{-3}	0.01	3.5^{-3}	7.7^{-4}	3.5^{-3}	3.9^{-3}	3.5^{-3}
80	0.2	1	2.0	-2.4^{-1}	4.2^{-3}	0.00	3.1^{-3}	-4.7^{-3}	3.1^{-3}	-1.0^{-2}	4.2^{-3}
80	0.2	2	0.1	-3.4^{-3}	4.2^{-3}	0.01	4.2^{-3}	-3.3^{-3}	4.2^{-3}	-1.9^{-3}	4.2^{-3}
80	0.2	2	1.0	-1.7^{-1}	5.2^{-3}	0.01	4.7^{-3}	-5.8^{-3}	4.6^{-3}	-1.1^{-3}	4.6^{-3}

Table C.3 continued

1	0.1	1	0.1	1.0^{-1}	2.8^{-2}	0.57	4.7^{-2}	1.1^{-1}	2.9^{-2}	3.0^{-1}	5.5^{-2}
80	0.2	2	2.0	-4.7^{-1}	6.9^{-3}	0.02	4.1^{-3}	3.1^{-3}	4.1^{-3}	-4.3^{-3}	5.9^{-3}
80	0.2	3	0.1	-5.9^{-3}	5.4^{-3}	0.01	5.5^{-3}	-5.8^{-3}	5.4^{-3}	-3.7^{-3}	5.4^{-3}
80	0.2	3	1.0	-2.6^{-1}	6.7^{-3}	0.02	5.6^{-3}	-4.8^{-3}	5.6^{-3}	3.4^{-3}	5.6^{-3}
80	0.2	3	2.0	-7.2^{-1}	1.0^{-2}	0.03	5.4^{-3}	5.5^{-4}	5.3^{-3}	-5.6^{-3}	7.5^{-3}
80	0.5	1	0.1	-1.5^{-3}	3.4^{-3}	0.01	3.5^{-3}	-1.4^{-3}	3.4^{-3}	-5.7^{-4}	3.4^{-3}
80	0.5	1	1.0	-8.7^{-2}	3.9^{-3}	0.01	4.0^{-3}	3.0^{-4}	4.0^{-3}	4.8^{-3}	4.0^{-3}
80	0.5	1	2.0	-2.4^{-1}	4.4^{-3}	0.01	3.5^{-3}	-7.3^{-3}	3.4^{-3}	-3.1^{-3}	3.4^{-3}
80	0.5	2	0.1	-3.1^{-3}	5.3^{-3}	0.02	5.5^{-3}	-2.8^{-3}	5.3^{-3}	-7.2^{-4}	5.4^{-3}
80	0.5	2	1.0	-1.8^{-1}	5.3^{-3}	0.02	5.0^{-3}	-7.3^{-3}	4.9^{-3}	1.3^{-3}	4.9^{-3}
80	0.5	2	2.0	-4.8^{-1}	7.2^{-3}	0.03	5.0^{-3}	1.7^{-4}	4.9^{-3}	8.0^{-3}	4.9^{-3}
80	0.5	3	0.1	-2.7^{-3}	6.7^{-3}	0.03	6.8^{-3}	-2.4^{-3}	6.7^{-3}	1.1^{-4}	6.7^{-3}
80	0.5	3	1.0	-2.6^{-1}	7.0^{-3}	0.04	6.7^{-3}	-4.3^{-3}	6.5^{-3}	8.9^{-3}	6.6^{-3}
80	0.5	3	2.0	-7.2^{-1}	1.1^{-2}	0.03	6.4^{-3}	-6.6^{-3}	6.3^{-3}	6.2^{-3}	6.3^{-3}

TABLE C.4: 95% confidence interval coverage rates for simulations with $n = 30$. The model included three slope parameters (β_p). Simulations varied the number of cases (c), the ratio of cases to controls (r), and the magnitude of the variance of the individual-specific random effect (σ_α). Methods used were the prospective logistic model (PLM), stratified case-control model (SCC), marginal logistic model (MLM), and the conditional logistic model (CLM). Superscripts indicate the exponents of scientific notation.

c	r	β_p	σ_α	PLM	SCC	MLM	CLM
1	0.1	1	1.0	0.95	0.95	0.95	0.97
1	0.1	1	2.0	0.87	0.87	0.88	0.99
1	0.1	2	0.1	0.95	0.73	0.95	0.95
1	0.1	2	1.0	0.91	0.79	0.91	0.97
1	0.1	2	2.0	0.71	0.81	0.73	0.99
1	0.1	3	0.1	0.96	0.64	0.97	0.99
1	0.1	3	1.0	0.89	0.68	0.89	0.97
1	0.1	3	2.0	0.63	0.75	0.66	0.97
1	0.2	1	0.1	0.96	0.87	0.96	0.99
1	0.2	1	1.0	0.93	0.94	0.93	0.95
1	0.2	1	2.0	0.92	0.89	0.94	0.98
1	0.2	2	0.1	0.95	0.83	0.95	0.96
1	0.2	2	1.0	0.94	0.94	0.94	0.96
1	0.2	2	2.0	0.82	0.86	0.84	1.00
1	0.2	3	0.1	0.97	0.78	0.97	0.99
1	0.2	3	1.0	0.95	0.82	0.95	0.99
1	0.2	3	2.0	0.71	0.80	0.74	0.99
1	0.5	1	0.1	0.96	0.95	0.95	0.96
1	0.5	1	1.0	0.93	0.93	0.93	0.98
1	0.5	1	2.0	0.89	0.97	0.86	0.99
1	0.5	2	0.1	0.96	0.98	0.95	0.96
1	0.5	2	1.0	0.99	0.97	0.99	0.98
1	0.5	2	2.0	0.81	0.98	0.78	0.97
1	0.5	3	0.1	0.99	0.98	0.99	0.95
1	0.5	3	1.0	0.98	0.98	0.98	0.98

Table C.4 continued

1	0.1	1	0.1	0.96	0.86	0.96	0.97
1	0.5	3	2.0	0.80	0.98	0.77	0.96
2	0.1	1	0.1	0.97	0.82	0.97	0.96
2	0.1	1	1.0	0.93	0.83	0.94	0.93
2	0.1	1	2.0	0.77	0.83	0.91	0.95
2	0.1	2	0.1	0.96	0.71	0.96	0.95
2	0.1	2	1.0	0.93	0.72	0.93	0.96
2	0.1	2	2.0	0.51	0.72	0.83	0.95
2	0.1	3	0.1	0.95	0.64	0.95	0.98
2	0.1	3	1.0	0.91	0.64	0.93	0.96
2	0.1	3	2.0	0.37	0.64	0.75	0.95
2	0.2	1	0.1	0.95	0.78	0.95	0.95
2	0.2	1	1.0	0.95	0.85	0.96	0.97
2	0.2	1	2.0	0.77	0.82	0.87	0.98
2	0.2	2	0.1	0.97	0.66	0.97	0.96
2	0.2	2	1.0	0.94	0.67	0.95	0.96
2	0.2	2	2.0	0.51	0.66	0.81	0.94
2	0.2	3	0.1	0.95	0.56	0.95	0.95
2	0.2	3	1.0	0.91	0.52	0.92	0.95
2	0.2	3	2.0	0.40	0.65	0.79	0.93
2	0.5	1	0.1	0.97	0.83	0.97	0.99
2	0.5	1	1.0	0.93	0.79	0.93	0.97
2	0.5	1	2.0	0.88	0.81	0.91	0.98
2	0.5	2	0.1	0.97	0.69	0.97	0.97
2	0.5	2	1.0	0.91	0.71	0.93	0.97
2	0.5	2	2.0	0.74	0.70	0.83	0.97
2	0.5	3	0.1	0.98	0.53	0.98	0.98
2	0.5	3	1.0	0.87	0.55	0.89	0.97
2	0.5	3	2.0	0.63	0.55	0.72	0.98
5	0.1	1	0.1	0.95	0.92	0.95	0.95
5	0.1	1	1.0	0.90	0.89	0.94	0.95
5	0.1	1	2.0	0.42	0.94	0.92	0.96

Table C.4 continued

1	0.1	1	0.1	0.96	0.86	0.96	0.97
5	0.1	2	0.1	0.96	0.85	0.96	0.98
5	0.1	2	1.0	0.83	0.89	0.92	0.95
5	0.1	2	2.0	0.11	0.90	0.92	0.96
5	0.1	3	0.1	0.94	0.81	0.94	0.96
5	0.1	3	1.0	0.80	0.82	0.93	0.99
5	0.1	3	2.0	0.07	0.86	0.90	0.97
5	0.2	1	0.1	0.95	0.91	0.95	0.95
5	0.2	1	1.0	0.95	0.90	0.94	0.96
5	0.2	1	2.0	0.51	0.86	0.93	0.92
5	0.2	2	0.1	0.94	0.79	0.94	0.91
5	0.2	2	1.0	0.83	0.87	0.90	0.96
5	0.2	2	2.0	0.25	0.79	0.91	0.93
5	0.2	3	0.1	0.95	0.81	0.95	0.95
5	0.2	3	1.0	0.77	0.84	0.90	0.95
5	0.2	3	2.0	0.12	0.75	0.87	0.93
5	0.5	1	0.1	0.94	0.85	0.94	0.94
5	0.5	1	1.0	0.92	0.85	0.94	0.96
5	0.5	1	2.0	0.67	0.87	0.95	0.98
5	0.5	2	0.1	0.97	0.83	0.97	0.95
5	0.5	2	1.0	0.86	0.73	0.88	0.91
5	0.5	2	2.0	0.33	0.74	0.87	0.93
5	0.5	3	0.1	0.95	0.73	0.95	0.96
5	0.5	3	1.0	0.86	0.67	0.90	0.95
5	0.5	3	2.0	0.21	0.73	0.82	0.91
10	0.1	1	0.1	0.94	0.94	0.94	0.95
10	0.1	1	1.0	0.79	0.98	0.95	0.97
10	0.1	1	2.0	0.26	0.92	0.95	0.97
10	0.1	2	0.1	0.95	0.92	0.96	0.95
10	0.1	2	1.0	0.70	0.93	0.95	0.96
10	0.1	2	2.0	0.03	0.89	0.95	0.94
10	0.1	3	0.1	0.94	0.93	0.94	0.94

Table C.4 continued

1	0.1	1	0.1	0.96	0.86	0.96	0.97
10	0.1	3	1.0	0.61	0.93	0.93	0.95
10	0.1	3	2.0	0.01	0.87	0.93	0.93
10	0.2	1	0.1	0.97	0.91	0.97	0.97
10	0.2	1	1.0	0.85	0.89	0.95	0.94
10	0.2	1	2.0	0.29	0.89	0.95	0.94
10	0.2	2	0.1	0.93	0.86	0.93	0.95
10	0.2	2	1.0	0.72	0.87	0.91	0.93
10	0.2	2	2.0	0.03	0.91	0.95	0.97
10	0.2	3	0.1	0.96	0.85	0.96	0.97
10	0.2	3	1.0	0.72	0.87	0.93	0.95
10	0.2	3	2.0	0.02	0.89	0.93	0.98
10	0.5	1	0.1	0.96	0.87	0.96	0.95
10	0.5	1	1.0	0.87	0.92	0.95	0.96
10	0.5	1	2.0	0.44	0.91	0.89	0.95
10	0.5	2	0.1	0.95	0.83	0.95	0.95
10	0.5	2	1.0	0.80	0.83	0.93	0.93
10	0.5	2	2.0	0.11	0.86	0.89	0.94
10	0.5	3	0.1	0.91	0.79	0.91	0.93
10	0.5	3	1.0	0.79	0.78	0.91	0.92
10	0.5	3	2.0	0.05	0.84	0.88	0.95
20	0.1	1	0.1	0.95	0.91	0.95	0.95
20	0.1	1	1.0	0.76	0.93	0.93	0.93
20	0.1	1	2.0	0.04	0.97	0.96	0.97
20	0.1	2	0.1	0.93	0.93	0.93	0.93
20	0.1	2	1.0	0.53	0.93	0.95	0.97
20	0.1	2	2.0	0.00	0.91	0.94	0.95
20	0.1	3	0.1	0.94	0.93	0.94	0.95
20	0.1	3	1.0	0.37	0.94	0.96	0.96
20	0.1	3	2.0	0.00	0.96	0.97	0.96
20	0.2	1	0.1	0.96	0.97	0.96	0.97
20	0.2	1	1.0	0.72	0.91	0.92	0.93

Table C.4 continued

1	0.1	1	0.1	0.96	0.86	0.96	0.97
20	0.2	1	2.0	0.07	0.94	0.95	0.95
20	0.2	2	0.1	0.98	0.95	0.98	0.99
20	0.2	2	1.0	0.59	0.95	0.98	0.97
20	0.2	2	2.0	0.01	0.93	0.94	0.96
20	0.2	3	0.1	0.95	0.91	0.95	0.96
20	0.2	3	1.0	0.41	0.92	0.95	0.96
20	0.2	3	2.0	0.00	0.93	0.93	0.97
20	0.5	1	0.1	0.93	0.91	0.93	0.93
20	0.5	1	1.0	0.81	0.94	0.94	0.95
20	0.5	1	2.0	0.13	0.90	0.93	0.95
20	0.5	2	0.1	0.97	0.93	0.97	0.95
20	0.5	2	1.0	0.67	0.89	0.90	0.93
20	0.5	2	2.0	0.01	0.91	0.94	0.95
20	0.5	3	0.1	0.92	0.85	0.92	0.95
20	0.5	3	1.0	0.61	0.86	0.92	0.93
20	0.5	3	2.0	0.00	0.91	0.92	0.96
80	0.1	1	0.1	0.97	0.97	0.97	0.97
80	0.1	1	1.0	0.25	0.95	0.95	0.94
80	0.1	1	2.0	0.00	0.98	0.98	1.00
80	0.1	2	0.1	0.99	0.97	0.99	0.99
80	0.1	2	1.0	0.05	0.95	0.96	0.96
80	0.1	2	2.0	0.00	0.93	0.93	0.75
80	0.1	3	0.1	0.97	0.96	0.97	0.97
80	0.1	3	1.0	0.05	0.94	0.93	0.95
80	0.1	3	2.0	0.00	0.96	0.95	0.75
80	0.2	1	0.1	0.95	0.93	0.95	0.95
80	0.2	1	1.0	0.38	0.89	0.88	0.89
80	0.2	1	2.0	0.00	0.93	0.95	0.96
80	0.2	2	0.1	0.95	0.94	0.95	0.93
80	0.2	2	1.0	0.12	0.91	0.93	0.93
80	0.2	2	2.0	0.00	0.95	0.95	0.93

Table C.4 continued

1	0.1	1	0.1	0.96	0.86	0.96	0.97
80	0.2	3	0.1	0.95	0.95	0.95	0.95
80	0.2	3	1.0	0.05	0.93	0.93	0.93
80	0.2	3	2.0	0.00	0.94	0.93	0.93
80	0.5	1	0.1	0.95	0.96	0.95	0.95
80	0.5	1	1.0	0.44	0.93	0.94	0.94
80	0.5	1	2.0	0.01	0.95	0.95	0.95
80	0.5	2	0.1	0.93	0.91	0.93	0.93
80	0.5	2	1.0	0.17	0.95	0.95	0.96
80	0.5	2	2.0	0.00	0.93	0.97	0.97
80	0.5	3	0.1	0.95	0.93	0.95	0.95
80	0.5	3	1.0	0.07	0.95	0.93	0.95
80	0.5	3	2.0	0.00	0.95	0.98	0.98