EXPERIMENTAL DESIGN FOR UNBALANCED DATA INVOLVING A TWO LEVEL LOGISTIC MODEL

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Abstract

The multilevel logistic model is used to analyze hierarchical data with binary outcomes, to detect variation both between and within clusters. I extended explicit variance formulae for a fixed effect in two level model for balanced binary data to account for imbalance both between and within clusters. The derivation of the variance is based on a linearization of the two level logistic model using first order marginal quasilikelihood (MQL1) estimation. In a simulation study, I used second order propensity quasilikelihood (PQL2) estimation to collaborate the accuracy of the analytic variance formula based on the observed racial distribution in a multi-center study of racial disparities. Using the site specific racial distributions, I simulated the log odds ratio for black race that could be detected with 80% power.

These methods are illustrated in the context of a multi-center study of racial disparities in 30-day mortality in the Veterans Affairs (VA) Healthcare System, where the racial distributions are dramatically unbalanced across the 149 sites. We also consider a subset of 42 sites that include a majority of the black hospitalizations. The same analytic variance is obtained when one has either equal numbers of observations per site and/or a constant proportion of black veterans across sites. The observed racial imbalance both within and across sites increases the variance of the race coefficient more in the Random Coefficient (RC) model than in the random intercept (RI) model. Compared to PQL2, the analytic variances using MQL1 are, severely downwardly

biased with smaller variance components. The simulation variances are virtually identical to the analytic variances for these data. For a given power, somewhat smaller log odds ratios can be detected in the RI model than in the RC model.

The derived formulas provide a basis for planning multi-center studies when a predictor of primary importance is highly imbalanced both between and within sites. In studies of racial disparities in health care, the site-specific population distributions are often known from administrative data. These methods for unbalanced data may facilitate more effective planning of public health relevant multi-center studies of racial disparities.

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PREFACE

During the preparation of this dissertation, I owe the following people my gratitude.

First, I give sincere thanks to Dr. Roslyn Stone, chair of my committee, for mentoring me through the PhD program with insightful suggestions, encouragement, constant support, unwavering patience, and invaluable input. I also express my appreciation to my committee members Dr. Michael J. Fine, Dr. Jong-Hyeon Jeong, Dr. Sati Mazumdar, and Dr. Ravi K. Sharma for their valuable suggestions, thoughtful comments, and guidance in this challenging undertaking.

I thank the Department of Biostatistics and the Center for Health Equity Research and Promotion (CHERP), which provided financial support through my Ph.D study, and Dr. Kevin Volpp for letting me join his racial disparity project. This project tremendously enriched my doctoral training and motivated the main idea of my dissertation.

I thank my friend in the Biostatistics Department for their kindness, laughter and help in my recovery from car accident. Their support has made my journey one of love, appreciation, and joy.

Finally, I thank and dedicate this work to my family. Without their love, encouragement and support, I could not have reached my ultimate goal.

I.   INTRODUCTION

A multilevel model(ML) is used to analyze the data with a hierarchical structure. Different statistics literature refers to the model with a variety of names: hierarchical model, mixed effect model, random effect model, random coefficient regression model, and covariate components model. As compared to a classic regression model, a multilevel model can take care of both heterogeneity and heteroscedasticity. Once multilevel models were developed, researchers applied this model more and more to the health service studies. The multilevel model with a binary outcome is one of the important models applied in medicine and health services research. An emerging issue is how to develop an appropriate experimental design for an unbalanced study using the multilevel logistic model. Unlike the estimation methods in the multilevel models, the experimental design in the multilevel logistic model causes only a few concerns. Under a balanced design, Moerbeek et al.[45] [50] have derived sample size formulae based on the variance formulae of the intervention as a fixed effect in the multilevel logistic model with or without a binary covariate. Simulation studies using different estimation methods verified their analytic results. I will extend these formulae to an unbalanced design in the context of a 2-level logistic model. This dissertation addresses variance and power in experimental design involving a two level logistic model and unbalanced data.

A.   STATEMENT OF PROBLEM

Because of the logit link in the multi-level logistic model and the existence of a random effect, it is difficult to derive the variance of fixed effect using the likelihood function. Currently, only the first order marginal quasi-likelihood (MQL1) can be used to derive the variance of

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the fixed effect, as in Moerbeek et al.[45] [50].

My primary aim is to derive the variance of the fixed effect of race in a two level random intercept (RI) or random coefficient (RC) logistic model for an observational study with dramatically unbalanced racial distributions both between and within sites. First, I derive the variance formulae of race, as a fixed effect in either a RI or a RC logistic model. The variance formulae are derived under the following six assumed design scenarios: 1) balanced within and across sites; 2) balanced across sites with the same sample weight (proportion black) within each site; 3) balanced across sites with site-specific sample weights; 4) unbalanced across sites and balanced within sites; 5) unbalanced across sites with the same sample weight within each site; and 6) unbalanced across and within sites with site-specific sample weights. Based on the analytic results, I will illustrate my methods using the site-specific racial distributions in the Volpp [34][76] study. To assess the impact of extreme imbalance, I will compare results based on (i) all site (complete data) to those based on (ii) a relatively small subset of sites that include 75% of the black veterans. The lowest quartile includes 108 sites (71.8%) that each hospitalize on average 31 black patients annually, while the largest quartile includes 9 sites (6.0%) that hospitalize on average of 377 black patients annually. I will compare analytic variance estimates under the six assumed design scenarios to empirical results. In a simulation study, the analytic results of variance formulae for both the RI and RC models will be compared to empirical results under alternative estimation methods.

My second aim is to estimate the target fixed effect parameter estimate that can be detected within power 0.8 through a simulation study. The target fixed effect estimates are compared for the RI model and RC models for the complete data as well as the higher black presence sites.

B.   MOTIVATING EXAMPLE

I have participated in the Volpp study [34][76] since it started in 2003. This study examines racial disparities in 30-day mortality within the VA for black and white veterans hospitalized from fiscal year(FY) 1996 to 2002 with one of six conditions: acute myocardial infarction

(AMI), congestive heart failure (CHF), gastro-intestinal bleeding (GI Bleed), hip fracture, stroke, or pneumonia. The Agency for Healthcare Research and Quality (AHRQ) considers these six conditions as important indicators of the quality of healthcare. Hospitalization is considered to be no-discretionary for AMI, hip fracture, and stroke, and discretionary for CHF, GI bleeding, and pneumonia. The primary data source is the hospital discharge data from the Veterans Affairs (VA) Patient Treatment File (PTF) for FY1996-2002 provide . The PTF contains information about primary and secondary diagnoses, age, gender, discharge disposition, transfer status, length of stay, patient zip codes, race and means test eligibility for every hospital discharge within the Veterans Health Administration. Date of death, available from the VA Beneficiary Identification Record Locator System File and verified by National Death Index, was linked to the PTF using encrypted social security numbers to ascertain mortality within 30 days of admission.

A number of studies within the VA Healthcare System (VAHS) has shown either better healthcare outcomes[11][33]or no racial disparities[28][31][19][60] in outcomes for black compared to white patients. This is inconsistent with extensive literature documenting racial disparities for civilian populations.

Although the reasons for the racial differences in the hospital care are not well understood, the following possible explanations, summarized in Volpp et al.[76] may offer some insight as to why black patients have better outcomes than white patients. First, black patients would rather be hospitalized than treated as outpatients; white patients have better access to outpatient treatment; Second, black patients are more likely to be admitted to the VAHS that have better average survival rates. Thus, blacks under age 65 will get a differential lower rate for private coverage in the VAHS, which increases the probability of a higher admission rate for blacks and a more positive outcome.

Several factors may explain the lack of disparities in outcomes within the VAHS[76]. First of all, black and white patients using the VAHS have relatively homogeneous socioeconomic status; this plays an important role in healthcare and leads to smaller racial disparities. Second, low income veterans, both black and white patients, access the same facilities and providers with essentially zero cost sharing. Meanwhile, the insurance status is highly correlated with race for non-VA hospitals. Most important, the military has played an important

role within American society in bringing about desegregation. The more equal treatment of racial minorities within the VA may reflect this improved integration of minorities within the military.

This project enriched my doctoral training and motivated my dissertation work. First of all, the racial distributions across sites have a dramatic imbalance. Table I.1 shows the quartiles of the site-specific average annual black patient volume. The lowest quartile includes 108 sites (71.8%) that each hospitalize on average 31 black patients annually, while the largest quartile includes 9 sites (6.0%) that hospitalize on average of 377 black patients annually. Second, Table I.2 shows five sites have zero mortality and 48 sites with no black deaths. These data provide a realistic example of imbalance between and within sites. Such racial distributional data are readily available to plan studies within the VAHS.

Table I.1: Distribution of VA Sites by Quartiles of Black Hospitalizations for Any of Six Conditions

Quartile of Black Hospitalizations	Number of Sites	Percentage of Sites	Mean Annual Black Hospitalizations
Q1	108	71.8	31.4
Q2	21	14.1	161.5
Q3	12	8.1	282.7
Q4	9	6.0	376.9
Total	150	100	90.5

Note: Quartile is defined by sorting the cumulative average annual
  number black visits from low to high

In my dissertation, I focus my example on pneumonia patients younger than 65, since hospitalization for pneumonia is considered discretionary following the AHRQ definition and represents veterans without Medicare. After excluding patients from the site without pneumonia hospitalizations, 149 sites were left. To compare the dramatically unbalanced design to a less unbalanced design, I use two data sets: 1)the complete data and 2) the data from the 42 sites (quartiles 2-4) that take care of 75% of black veterans. Table I.2 lists the

site- and race-specific numbers of deaths and corresponding death status by quartile of black patient volume.

Table I.2: Site and Race Specific Mortality for Veterans
Aged <65 Years and Hospitalized with Pneumonia

Volume	Site	Black Deaths	Total Blacks	White Deaths	Total Whites
1	1	0	2	6	100
1	2	0	0	10	122
1	3	0	1	3	104
1	4	0	5	14	130
1	5	0	3	21	198
1	6	0	2	1	73
1	7	2	15	10	113
1	8	2	63	16	123
1	9	1	23	11	151
1	10	1	14	13	181
1	11	6	69	19	166
1	12	0	1	6	93
1	13	4	21	20	243
1	14	2	36	15	236
1	18	0	5	0	7
1	19	0	3	3	47
1	20	3	35	35	406
1	21	2	20	20	237
1	22	1	4	4	68
1	23	1	39	10	156
1	25	3	66	22	293
					Continued on next page

Table I.2 – Continued from previous page

Volume	Site	Black Deaths	Total Blacks	White Deaths	Total Whites
1	26	0	14	6	86
1	29	3	63	20	199
1	30	1	8	2	33
1	31	1	13	8	91
1	32	1	6	6	74
1	33	0	0	3	44
1	34	0	1	14	220
1	40	0	3	11	182
1	42	0	7	18	215
1	45	3	57	21	233
1	47	1	19	13	160
1	48	2	72	9	198
1	50	5	71	9	283
1	51	1	5	8	118
1	52	2	45	4	91
1	53	9	77	8	177
1	56	1	8	2	20
1	57	1	5	2	81
1	58	0	2	12	240
1	60	0	0	2	70
1	61	0	2	0	27
1	62	0	15	13	140
1	63	7	75	29	321
1	64	2	26	6	137
1	65	0	2	5	70
1	67	0	0	0	6
					Continued on next page

Table I.2 – Continued from previous page

Volume	Site	Black Deaths	Total Blacks	White Deaths	Total Whites
1	69	0	12	20	237
1	71	1	7	13	172
1	72	0	0	4	78
1	75	0	3	3	40
1	76	0	1	3	21
1	77	0	4	0	16
1	78	0	3	1	19
1	79	9	114	4	96
1	81	1	22	6	165
1	82	6	30	7	92
1	83	2	30	8	86
1	84	0	2	1	27
1	88	0	1	0	5
1	89	1	58	37	333
1	90	1	10	11	204
1	91	0	0	7	88
1	92	0	15	9	141
1	93	0	6	6	34
1	94	3	36	10	195
1	96	0	14	22	314
1	98	3	41	3	30
1	99	0	11	16	240
1	100	2	27	10	119
1	101	2	24	12	185
1	103	2	12	4	60
1	107	1	47	10	244

Table I.2 – Continued from previous page

Volume	Site	Black Deaths	Total Blacks	White Deaths	Total Whites
1	108	8	68	32	422
1	109	1	34	12	214
1	110	0	2	6	76
1	111	0	2	9	74
1	112	0	9	18	169
1	113	3	42	25	267
1	115	3	94	34	597
1	117	1	2	8	112
1	118	1	18	22	428
1	119	0	1	11	141
1	120	1	17	13	189
1	122	0	1	12	121
1	123	0	6	6	136
1	124	1	14	11	115
1	126	0	2	4	44
1	127	3	48	16	228
1	128	0	10	35	331
1	130	2	37	25	357
1	131	0	20	4	165
1	132	3	98	27	355
1	134	0	6	10	117
1	135	1	17	4	102
1	136	6	64	22	288
1	137	0	0	6	87
1	138	8	109	38	498
1	140	1	8	8	84

Table I.2 – Continued from previous page

Volume	Site	Black Deaths	Total Blacks	White Deaths	Total Whites
1	141	0	12	4	38
1	142	0	22	24	290
1	143	1	13	0	7
1	144	1	3	2	38
1	145	0	0	7	60
1	147	8	79	20	179
1	149	0	12	5	100
1	150	6	82	14	216
2	16	9	124	24	225
2	35	18	172	14	223
2	39	4	106	34	319
2	43	13	188	18	207
2	44	11	267	14	209
2	54	18	139	19	196
2	59	5	117	6	110
2	66	12	161	27	317
2	70	4	116	33	353
2	74	7	118	29	291
2	85	9	116	26	388
2	86	5	105	34	306
2	87	4	84	24	361
2	97	13	95	9	84
2	102	5	159	24	386
2	105	7	205	5	157
2	106	6	65	3	55
2	116	5	77	17	237
					Continued on next page

Table I.2 – Continued from previous page

Volume	Site	Black Deaths	Total Blacks	White Deaths	Total Whites
2	129	5	136	24	269
2	133	10	91	13	192
2	139	12	103	17	284
3	15	19	310	21	273
3	24	28	171	25	286
3	27	12	231	6	96
3	28	4	134	4	76
3	36	2	39	4	34
3	38	9	141	6	91
3	41	20	226	20	317
3	49	18	275	5	114
3	55	15	279	6	89
3	73	25	138	26	178
3	114	19	245	7	101
3	148	22	320	64	537
4	17	21	493	11	176
4	37	31	541	2	61
4	46	21	233	46	490
4	68	34	347	51	574
4	95	27	245	20	228
4	104	18	225	14	141
4	121	33	282	31	298
4	125	7	205	29	236
4	146	22	488	5	80
Total	149	750	10,817	2,028	26,294

I have organized my dissertation as follows. After introducing the problem and motivating example in the first chapter, I give a literature review of experimental design on the multilevel linear model and the multilevel generalized linear model in Chapter Two. My analytic methods and simulation algorithm are describe in Chapter three. These methods focus on detecting the racial disparities in an unbalanced multilevel logistic model, where race could be estimated as a fixed effect or a random effect in the model. The analytic and simulation results are summarized in Chapter Four, while the final chapter presents the conclusions and discussion. In the Appendices A to C, I attach the lists of acronyms, glossary and mathematical notation, respectively. The derivation is reported in Appendix D, step by step. I show the screen images of model fitting results using MLwiN in Appendix E, which is followed by the bibliography.

II. LITERATURE REVIEW

After I review the Volpp study, which is using the two-level logistic model to detect racial disparities across sites, I will review the literature of experimental design for MLM. I will explain the multilevel logistic model (MLLM) using different notation, present estimation methods, review hypothesis test algorithms for random and fixed effects, and compare estimation methods and hypothesis test algorithms in MLLMs. The literature on experimental design in MLLMs with balanced data will be reviewed. Then, sample size issues in a two-level logistic model with balanced or unbalanced design using MCMC simulation will be outlined. Feiveson's simulation algorithm on post hoc power, which calculates the cumulative proportion of rejections from multiple replications of the experiment, will be reviewed in the last section.

A. THE VOLPP STUDY

I have participated in the VA HSR&D funded Volpp study since it started in 2003. This project has several phases. I will summarize the phases that are relevant to this dissertation. The first phase focused on the relationship between racial disparities and patient characteristics. Another phase focused on the relationship between the racial disparities and hospital characteristics. Both phases are using the same observational dataset, which has known unbalanced sample sizes and racial distributions across sites.

The first phase phase of Volpp study[76] examined racial disparities in 30-day mortality within the VA for white and black veterans hospitalized from fiscal year(FY) 1996 to 2002 with one of six conditions. For each of the six study conditions, unadjusted 30-day mortality

rates were significantly lower for blacks than for whites (p<0.01). These results did not vary after adjusting for hospital site where treated or more complete ascertainment of deaths. There were no significant changes in the degree of difference in mortality by race following quality improvement efforts within VA during the study period. The finding that black veterans have significantly lower 30-day mortality than white veterans for the six common conditions generally is limited to veterans over age 65. This differential by age suggests that it is unlikely that lower 30-day mortality rates among blacks within the VA are driven by treatment differences by race. For veterans with pneumonia younger than 65 years old, the variance component of race has the largest value (0.094).

Another phase of Volpp project, as reported by Jha et al.[34], focuses on racial disparities on 30-day mortality by quartile of the relative number of black patients hospitalized at each site. This is quantified in term of the average annual number of black patients hospitalized at each site over the study period. These site-specific number are sorted, in increasing order, and the first quartile is defined as the sites that hospitalized 25% of black patients. The forth quartile includes a much smaller number of sites with relatively large numbers of black patients. The racial distributions across sites are dramatically unbalanced, as shown in Table I.1. By adjusting for quartile of black patient volume, we compare the racial disparities across sites with different race distributions. The hospitals that care for most black patients are more likely to be urban teaching hospitals and to have more technologically advanced equipment. The lack of variation in 30-day mortality and in racial disparities across these hospitals is surprising, and suggests more uniformity in care within VA than in the private sector.

B. MULTILEVEL MODELS

Hierarchical, nested, or clustered structure is a common phenomenon in social or healthcare research[25][57][63]. For example, a cluster could be children coming from the same family or in the same classroom, patient in the same hospital and/or treated by the same physician. These examples share a pattern that a lower level is nested within a higher one, for instance, children nested within a family or classroom, or patients nested within a physician and/or hospital. The hierarchical data could have 2 or more levels. Two-level or three-level data structures are commonly used in statistical analysis, to avoid even more complicated variance covariance structures. Different authors refer to level one as the highest level or the lowest level of the clustering. I will follow Goldstein's definition[25], and call the individual level level one, which may be referred to as i_{th} level (i=1, $\ldots$, n_j). Similarly, the j_{th} level is refered to as the j_{th} cluster (or group), where j=1, $\ldots$, N. Thus, y_{ij} is the outcome for the i_{th} individual in the j_{th} cluster.

Based on the type of outcome variable, multilevel models are be categorized as either MLMs (in continuous outcomes) or multilevel generalized linear models (MGLM) (for discrete outcomes). For MLMs, the response variable and the residuals in each level follow normal distributions. For MGLMs, the residuals and response variable might follow normal distribution if we standardize the model using the link function. Otherwise, they will follow different exponential distribution. Based on different link functions for the outcome variable, MGLMs includes a MLLMs, multilevel possion models, multilevel multinominal models, and multilevel ordinal models. Based on the specified variance-covariance structure of the MLM, each of the specified MLMs includes RIs and possibly RCs. More complex multilevel models include multivariate multilevel models (with multiple outcome variables) and multiple membership models (where membership varies by levels). Other latent variable models, multilevel factor analysis, structure equation model, and cross-classified model also can be formulated as multilevel models.

The multilevel model is used to analyze data with a hierarchical structure to account for the relationships within and between levels. As a generalization of classic linear regression, the multilevel model can: estimate the main effects and interaction effects within or across

levels; reduce the bias in parameter estimates from clustering; provide appropriate standard errors to correct confidence intervals and hypothesis tests for clustering; and decompose the total variance into portions within each level of the model.

C. EXPERIMENTAL DESIGN IN LINEAR MODELS

Experimental design, as one of the important steps in designing a study, has been the focus of a lot of research. The rule of thumb for a study design is to increase precision and eliminate bias. Therefore, sample size estimation will assures a maximum degree of precision for parameters being estimated (min type I error, α) and assures a minimum type II error for a specified type I error and a specified point in the alternative hypothesis (max power). The statistics power is 1-type II error (1-β). Researchers present more and more research for experimental design with correlated observational studies.

1. Two-Group Comparison for Single Level

Fleiss[18] summarizes the experimental design under different situation. The sample size formula for an observation study, using the general form of two-group t-test sample size, under the hypothesis test $H_0 : \mu_1 = \mu_2$ vs. $H_1 : \mu_1 \neq \mu_2$, can be written as below

$$N = \frac{(\text{Error Terms})(Variance)}{(\text{Difference to be Detected})^2}. \tag{II.1}$$

Assuming we have two group x and y, the group mean for group x and group y are μ_1 and μ_2 with variance σ_1^2 and σ_2^2, respectively. The type one error is denoted as α. The type two error is β. In Equation (II.1), N is total sample size; Error terms is the square to the sum of inverse cumulative normal distribution for type I and type II error $((Z_{\frac{\alpha}{2}} + Z_\beta)^2)$; Variance is the sum of group variances. When groups share the same variance (σ^2), the Variance in the equation is $2\sigma^2$. When the two group are correlated, the variance for these group have a correlation coefficient ($\rho = \frac{\sigma_1^2}{\sigma_2^2}$). The difference to be detected is the different for two group

mean ($\delta = \mu_1 - \mu_2$). For normal distributed data with common variance, we can write the sample size with common variance as

$$N = (Z_{\frac{\alpha}{2}} + Z_{\beta})^2 \frac{2\sigma^2}{\delta^2}. \tag{II.2}$$

For normal distributed correlated data with common variance, the sample size formula is

$$N = (Z_{\frac{\alpha}{2}} + Z_{\beta})^2 \frac{2\sigma^2(1-\rho)}{\delta^2}. \tag{II.3}$$

For normal distributed uncorrelated data with different variance, we can write the sample size with common variance as

$$N = (Z_{\frac{\alpha}{2}} + Z_{\beta})^2 \frac{\sigma_1^2 + \sigma_2^2}{\delta^2}. \tag{II.4}$$

For normal distributed correlated data with different variance, the sample size formula is

$$N = (Z_{\frac{\alpha}{2}} + Z_{\beta})^2 \frac{(\sigma_1^2 + \sigma_2^2 - 2\sigma_1\sigma_2)}{\delta^2}. \tag{II.5}$$

By changing the location of N, we can get the generalized powe formula

$$Power = 1 - \Phi^{-1}[\frac{\text{N * difference to be detected}}{variance} - Z_{\frac{\alpha}{2}}]. \tag{II.6}$$

The Φ^{-1} is the probability under a specific value using normal distribution.

The above equations involve four elements 1) sample size, 2) standard deviation, 3) Type one and two errors, and 4) sample size mean in each group. By knowing three of the four elements, the other element can be calculated. A balance is needed between minimized standard error and maximum power.

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2. Experimental Design in Multilevel Linear Models

In experiment design for MLMs, optimal allocation of experimental units, optimal sample size, and power have been investigated for balanced data. Tan and Bosker[75] and Hedeker et al.[30] presented optimal experimental design in the repeated measures. Setting the optimal randomization level as the individual level in the intervention study had been reported by Donner et al.[12], Gail[20], and Moerbeek[46][48]. The optimal sample size for each level, given randomization level, measurement method, and budget, has been derived by several authors. Specifically, in the 2-level linear model, sample size formulae for an intervention randomized at the group level have been discussed [1][14][12][16][32][37][39][61]. Raudenbush and Liu[55]derived sample size calculations for cluster randomization with or without a covariate, based on Raudenbush's work[54] for cluster randomization trials . Appropriate software, Optimal Design[65], was developed at the same time. Snijders and Bosker[62] did an approximate study of standard errors of the fixed terms with or without covariates and/or budget constrains for the 2-level variance component linear model. They recommended that the sample size for the group level should be as large as possible. Based on this, Snijders developed a comprehensive package PINT[3] to calculate the sample size for the fixed term in the 2-level linear model with balanced data with or without covariates. For both levels, the number of independent variables can vary. Raudenbush[54], Raudenbush and Liu's[55] case are a special case of Snijders and Bosker. Mok[51] did a simulation study for a 2-level linear model to compare designs when the number of individuals is larger than, equal to, and smaller than the number of clusters. Hsieh[32] and Donner et al.[12] give the formula for the power to detect an intervention effect in a of 2-level cluster randomized study with a given sample size under balanced design.

Moerbeek et al.[46] address 1) optimal level of randomization, 2) optimal allocation of units, and 3) optimal sample size for a given budget and level of randomization of intervention in balanced 2-level and 3-level linear models with or without a covariate. Covariates have an effect on the intervention through their effect on unexplained variance. Therefore, we should take covariates into account at the design stage. Moerbeek et al.[48] discuss optimal experimental design for 2- or 3- level MLM with a covariate, when the intervention was

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randomized at the cluster or individual level. In this paper, she reports that pre-stratification on the covariate leads to a more efficient design, and that the optimal level of randomization is the lowest level.

D.   MULTILEVEL MODELS WITH DISCRETE OUTCOMES

More and more applications of multilevel models are appearing in healthcare research. MLLMs are used for data with binary outcomes. For example, healthcare satisfaction or 30 day mortality could be treated as binary outcomes. In this dissertation, I limited my study to 2-level logistic models without covariates.

1.   2-level Logistic Models

We can write multilevel model[24] in several ways as a, 1) generalized model, 2) combined model, and 3) standard model. Another omit style, level-specific model exist and won't be discussed in this dissertation. Here, I will introduce the two level logistic model in the above three styles, which are related to my variance derivation. These models can be applied to a study with a population of $M = \sum_j n_j$ samples. Within the population, the i_{th} individual $(i = 1, \ldots, n_j)$ is nested in j_{th} group $(j = 1, \ldots, N)$. The binary outcome variable is denoted as $\mathbf{Y}_{ij}$, which is assumed to follow binomial distribution, where π_{ij} is the probability that the response for the i_{th} individual in the j_{th} group is equal to one (so $\pi_{ij} = pr(\mathbf{y}_{ij} = 1)$). For the logistic model, the link function, $\mathrm{logit}(\pi_{ij})$, is equal to $\log(\pi_{ij}/(1 - \pi_{ij}))$. E is the error term in the model, and n_{ij} is the denominator for the empirical proportion.

A generalized combined 2-level logistic model can be written as (II.7)

$$logit(\pi_{ij}) = (X\beta)_{ij} + (Z\mu)_j + E_{ij}$$
$$\text{where} \quad y_{ij} \sim BIN(\pi_{ij}, n_{ij}) \quad \text{and} \quad var(y_{ij}|\pi_{ij}) = \pi_{ij}(1 - \pi_{ij})/n_{ij},$$
$$X = [X_{ij}], \quad X_{ij} = \{x_{0ij}, x_{1ij}, \ldots, x_{pij}\},$$
$$E = \{e_{ij}\} = E_1 + E_2 = \{e_{ij}^1 + e_{ij}^2\}, \quad e_{ij}^1 = e_{ij}, \quad \text{and} \quad e_{ij}^2 = \mu_j$$

$$\text{(II.7)}$$

The standard representation for a $2-$level generalized logistic model including the level 1 variation is (II.8)

$$y_{ij} = \pi_{ij} + e_{ij}z_{ij} = f(H) + e_{ij}z_{ij},$$
$$\text{where} \quad z_{ij} = \sqrt{\pi_{ij}(1 - \pi_{ij})/n_{ij}} \ ,$$
$$\sigma_e^2 = 1,$$
$$\text{and } \pi_{ij} = [1 + exp(-(X\beta))]^{-1}.$$

$$\text{(II.8)}$$

After calculation, the variance of β_1 are summarized in below table.

Instead of presenting the model in a generalized representation, I will present the RI and RC logistic model in the combined representation. These models are shown in terms of the variables for the Volpp study in (II.9) and (II.10), respectively, for the RI and RC models.

$$logit(\pi_{ij}) = \beta_0 + \beta_1 x_{ij} + \mu_{oj} + \varepsilon_{ij} \tag{II.9}$$

$$logit(\pi_{ij}) = \beta_0 + \beta_1 x_{ij} + \mu_{oj} + \mu_{1j} x_{ij} + \varepsilon_{ij} \tag{II.10}$$

In these models, π_{ij} is the mortality from any source; β_0 is the average intercept across the sites; β_1 is the average regression slope across the sites; x_{ij} is a dummy variable for black race, the only independent variabel, coded as 1 for black veterans and 0 for white; μ_{oj} is the unique increment to the intercept associated with the j_{th} site; and μ_{1j} is the unique increment to the slope associated with j_{th} sites. Both μ_{oj} and μ_{1j} are called level 2 residuals; ε_{ij} is the level one residuals. Brown and Prescott[4] and Snijder [63] called the slope term $(\mu_{1j} x_{ij})$ in (II.9), which represents heterogeneity between sites in the effect of race, as the site-by-race interaction term(site ● race). Following Goldstein's[24] definition, I will call this term "race as random effect". To do quasi-likelihood estimation, we need to write models (II.11) and (II.12) in a standard way as, respectively, for the 2-level RI and RC model.

$$y_{ij} = f(H) + \varepsilon_{ij} = f(\beta_0 + \beta_1 x_{ij} + \mu_{oj}) + \varepsilon_{ij} \tag{II.11}$$

$$y_{ij} = f(H) + \varepsilon_{ij} = f(\beta_0 + \beta_{1j} x_{ij} + \mu_{oj} + \mu_{1j} x_{ij}) + \varepsilon_{ij} \tag{II.12}$$

2.   Estimation Methods and Hypothesis Tests for 2-level Logistic Models

When I denote the 2-level logistic model as model (II.7), the response variable (y_{ij}) does not follow a normal distribution. Instead, the response estimations follow logistic distribution and are dependent on the the random term in the model. Therefore, we cannot directly use the maximum likelihood estimate method, which was used for the MLM. To estimate the parameter, researchers developed estimation methods using a modified maximum likelihood estimate (MLE), a sampling method, and a Bayesian method. Based on extended MLE method, Fisher Score[57], the Expection-maximization (EM) Algorithm[57], Fisher scoring combined with EM algorithm[57], and Quasi-likelihood[25], were developed. Numerical integration methods can be applied as in Laplace[57] and Gauss-Hermite quadrature [43]. Goldstein et al.[27] developed a bootstrap sampling method. Markov Chain Monte Carlo (MCMC) method[5] is a Bayesian method.

Extensions of the quasi-likelihood estimation have been implemented in the software MlwiN[70]. The marginal quasi-likelihood estimate method (MQL) has also been implemented in S+[74], while the propensity quasi-likelihood estimate (PQL) method has been incorporated in software SAS(proc GLIMMIX)[67], R(glmmPQL)[73], S-Plus, Mplus[71], and HLM[57]. Goldstein[27] also developed the non-parametric and semi-parametric iteration bootstrap method in MLwiN. Browne[5] implemented the MCMC method by using Gibbs sampling; MetropolisCHastings (MH) sampling for MGLM in MLwiN. Raudenbush, Yang, and Yosef [56] developed the Laplace method, Fisher scoring, and the EM algorithm for the multileve logistic model and implemented them in HLM; McCulloch and Searle[43] developed the Gauss-Hermite quadrature approxach for MGLM. This method has been implemented in SAS (proc nlmix), AML[66], MIXOR [69], and Stata (xtlogit or gllamm)[68]. Next subsection describe the quasi-likelihood methods, particularly MQL1. These methods will be compared later.

a.   Propensity Quasi-likelihood and Marginal Quasi-likelihood Estimation

The quasi-likelihood method applies the Talyor expansion of a standardized logistic model to estimate π on the $(t+1)_{th}$ iteration, using t_{th} estimates. PQL and MQL, commonly used

estimation methods for MGLM, take different approaches using quasi-likelihood methods. Depending on the order of the Taylor extension on f(H) in the standardized MLLMs, MQL1 or PQL1 are obtained using the first order in MQL or PQL, respectively; similarly, MQL2 and PQL2 use the second order of the Taylor extension. Estimating the fixed effect using full maximum likelihood method (FML)gives the corresponding iterative generalized least squares (IGLS) PQL or MQL estimates. Estimating the fixed effect using the restricted maximum likelihood method (REML)gives the corresponding restricted iterative generalized least squares (RIGLS) PQL or MQL estimates. Therefore, the quasi-likelihood method can be split to IGLS MQL or RIGLS MQL, and IGLS PQL and RIGLS PQL. Including the adequate of the Talyor series expansion, there are eight quasi-likelihood methods: RIGLS MQL1, RIGLS MQL2, IGLS MQL1, IGLS MQL2, RIGLS PQL1, RIGLS PQL2, IGLS PQL1, and IGLS PQL2. The main steps for the quasi-likelihood estimation are shown below, stating with model.

First of all, the π_{ij} in model (II.8) is expressed as

$$\pi_{ij} = f(X\beta + Z\mu) = f(H) = [1 + exp(-(X\beta + Z\mu))]^{-1} \qquad (\text{II.13})$$

the $(t+1)_{th}$ iteration estimates of random and fixed parts are obtained using the estimates in the t_{th} iteration through the 2nd order Taylor series of π_{ij} as

$$
\begin{aligned}
f_{ij}(H_t) - X_{ij}\beta_t f'_{ij}(H_t) + (Z_{ij}\mu_j)f'_{ij}(H_t) + X_{ij}\beta_{t+1}f'_{ij}(H_t) \\
+ (Z_{ij}\mu_j)^2 f''_{ij}(H_t)/2 + (Z_{ij}\mu_j)^2 f{ij}''(H_t)/2
\end{aligned}
\qquad (\text{II.14})
$$

When we choose $H_t = X_{ij}\beta_t + Z_{ij}\widehat{\mu}_j$, and plug in the estimate of β_t, $\beta_{(t+1)}$, and $\widehat{\mu}_j$ from IGLS or RIGLS, this method is called PQL2. If we take the first order Taylor series instead of the second order, it is PQL1. Using $H_t = X_{ij}\beta_t$ (assuming $\mu_j = 0$ at t_{th} iteration)gives MQL. MQL or MQL2, respectively, use the first or second order Talyor series of π_{ij}. I summarize these four methods in Table (II.1).

Within the MQL and PQL methods, the first order Taylor series is not as accurate as the second order. The MQL method will give severe underestimates and is not good at convergence, especially when n_{ij} is small. The PQL1 method is better in terms of point estimation, but is not good for testing. PQL2 estimates approach the true values based on

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Table II.1: Definition of H_t for the MQL and PQL methods

ML Method	H_t in (II.14)	Taylor Series order	Quasi-likelihood method
FML	$H_t = X_{ij}\beta_t$	1	IGLS MQL1
FML	$H_t = X_{ij}\beta_t$	2	IGLS MQL2
FML	$H_t = X_{ij}\beta_t + Z_{ij}\widehat{\mu}_j$	1	IGLS PQL1
FML	$H_t = X_{ij}\beta_t + Z_{ij}\widehat{\mu}_j$	2	IGLS PQL2
REML	$H_t = X_{ij}\beta_t$	1	RIGLS MQL1
REML	$H_t = X_{ij}\beta_t$	2	RIGLS MQL2
REML	$H_t = X_{ij}\beta_t + Z_{ij}\widehat{\mu}_j$	1	RIGLS PQL1
REML	$H_t = X_{ij}\beta_t + Z_{ij}\widehat{\mu}_j$	2	RIGLS PQL2

a simulation study[26] and seems be perform best in the quasi-likelihood estimation. When PQL2 does not converge, Goldstein [24] suggests using MQL2. Moerbeek et al.[45] give similar recommendation as Goldstein[24]. RIGLS is required when there is a small sample size. The deviance estimates from these methods are very crude. We cannot apply the deviance to perform hypothesis test from any of these methods. Mlwin user Manual [53] has point out quasi-likelihood method is good at exploring model and computation intensive algorithm, MCMC, will give an accurate estimations.

b.   Hypothesis Tests for Multilevel Generalized Linear Models

Because of existence of link function and random effect, it's difficult to get estimate of variance of fixed effect. The optimal hypothesis test ($H_O : K'B = 0$) in MGLMs is an open research area[25]. So far, we can split the test into a main effect or a pairwise test according to the definition of K'B. Using test terms, we can perform non-predictor involved hypothesis tests (heterogeneity of proportions) and predictor related hypothesis test. Specifically, random intercepts and random coefficients in MGLMs. First, I will summarize the hypothesis test on heterogeneous proportions.

Test of Heterogeneous Proportions

In the absence of predictors, we can summarize response proportion by cluser in the contingency tables. The Chi-square test can be applied to these variables whose contingency table cells are all greater than 1 and 80% larger than 5. Thus, a Chi-squared test, with an N-1 degree of freedom, will be used to test the differences between groups.

Commenges and Jacqumin[8] reported another test statistics to test the heterogeneous across the clusters.

$$T = \frac{\sum_{j=1}^{N}\{n_j^2(\bar{Y}_{.j} - \hat{P}_.)^2\} - M\hat{P}_.(1 - \hat{P}_.)}{\hat{P}_.(1 - \hat{P}_.)\sqrt{2\sum_{j=1}^{N} n_j(n_j - 1)}} \tag{II.15}$$

In (II.15), T follows normal distribution. Commenges' method has higher power than chi-square test, when it is used to test heterogeneity of site-specific proportions without any model fitting. We can apply this method to a sample when the group size is larger than 10 and when there is no dominator group, ie. $n_j/M <= .1$ and $n_{jmax}/n_{jmin} <= 10$.

Tests of Fixed Effects and Random Effects

For MLM, a test for the fixed effect can be completed using a t- test, Wald test, deviance test[56] [63], or score test[38]. The deviance test can not be applied to quasi-likelihood method, since their results are crude.

a. Hypothesis Test for Fixed Effect

By obtaining the parameter estimates and variance, a A t-test II.16 can be used to test a single fixed effect parameter equal to 0m ($H_o : \beta_i = 0$) as shown below.

$$t_{n_i-r_i-1} = \hat{\beta}_{ij}/SE_{\hat{\beta}_{ij}} \tag{II.16}$$

By assuming there are n_i units and r_i explanatory variables in the level i, the degree freedom for level i is $n_i - r_i - 1$. This t-test will follow a t-tes with$n_i - r_i - 1$ degree freedom.

The quantile estimates test can be applied when we using bootstrap or MCMC estimation[53]. The accuracy of $(1 - \alpha)$ confidence interval of this quantile estimates test depend upon iteration number. Davison and Hinkley[10] suggested repeat number should be, at least, 1000.

Both Wald test and likelihood ratio test can perform the multi-parameter hypothesis test as a special case of linear function of fixed effect ($H_o : f = C\beta = k$). C is a r*p contrast matrix, which defined the linear function of the p parameters. Wald tests [25] can be used for the following situation:

I. Omnibus tests of the relationship between a categorical higher level predictor and higher level specific parameter.

II. Contrast between categories of a higher level predictor.

III. Examining cross level interation.

IV. Examining whether some subset of cluster level predictors is needed in a particular lower level model.

Based on the hypothesis test, we will obtain an approximately χ^2 distribution(II.17) with r degree freedom in the Wald test.

$$R = (\hat{f} - k)^T [C(X^T \hat{V}^{-1} X)^{-1} C^T](\hat{f} - k) \tag{II.17}$$

Where $\hat{f} = c\hat{\beta}$ and $(X^T \hat{V}^{-1} X)^{-1}$ is estimated covariance covariance matrix of fixed effect.

When we set $\hat{R}$ equal to α, the tail region of the χ_r^2 distribution in (II.17), we can get a simultaneous (100-α)% confidence interval for the i_{th} row of C as ($C_i\hat{\beta} - d_i$, $C_i\hat{\beta} + d_i$). The d_i is $C_i(X^T \hat{V}^{-1} X)^{-1} C_i^T \chi_{q,(\alpha)}^2$.

Likelihood ratio test(also called deviance test) is another options for fixed effect and will obtain similar result as Wald test. This method is applicate on multiple parameters test and random effect test when K is zero. Comparing Wald test to deviance test, there are three advantages for Wald test: 1)can perform any linear test within the the alternative model of likelihood ratio test, 2)perform any linear contrast to fixed effect, and 3)can be used for REML method, which has applicable limitation for likelihood ratio test. When λ_0 is denoted for the likelihood of the null hypothesis, λ_1 is denoted as likelihood of alternative hypotheses, and q as the different number of parameter between the null hypothesis and alternative hypothesis, we can write the deviance statistics or log likelihood ratio D_{01} as (II.18)

$$D_{01} = -2log\lambda_0/\lambda_1 \tag{II.18}$$

. The hypothesis test follows a chi square distribution with q degrees freedom.

For multiparameter test, we can also use Bayesian deviance information criterion(BDIC) method to perform the test in MCMC method. Within each chain of MCMC, we computer -2log-likelihood of the model being fitted using current chain value, D_i, and the mean -2log-likelihood as $\bar{D}$. Upon convergence, we can get deviance as D. The DIC will be $D+2*(\bar{D}-D)$, where $(\bar{D}-D)$ is called effective number of parameters.

b. Hypothesis Test for Random Effect

Goldstein[25] mentioned Wald test can be used for the random effect when sample size is large enough. Likelihood ratio test is preferred for the random effect. We need caution that we can and only can compare the models with same fixed effect for REML. Emphatically, the deviance test is exceeding the nominal values, very liberal, unless the cluster size is large enough. Therefore, we need use IGLS method when we need do hypothesis test on random effect. We can perform score test [38] in MLLMs'. The hypothesis test on the random effect in the MLLMs is an open research area[25]. We assumed normality of residual, we can apply t test to the residual we are going to exam. Based on this, we also can draw the caterpillar plot to check the normality and find outliers of cluster. Quantile estimates test and BDIC test can be applied to the random effect hypothesis test.

3.   Estimating method and hypothesis test comparisons in MGLMs

Within the estimate methods, MLM, IGLS, RIGLS, EM, Fisher Scoring, EM & Fisher scoring are iterated maximum likelihood methods. Because of the complicated structure of multilevel model, it is difficult to find an estimation method to get accurate parameter estimates. The iterative maximum likelihood method will get biased estimate. Part of them will get the estimate of variance out of parmeter space. If we want to explore the model, the best choice to get the estimate will be IGLS, RIGLS, or EM plus Fisher scoring method. If we want get accurate estimates for MLM, MCMC method and bootstrap will be our choice. On one side, MCMC method is the most computationally intensive, which requires several hours to fit a model. On the other side, it will give us an approximate unbiased estimate, no matter where prior distribution and initial values are assumed. This has the advantage in

small samples, that MCMC takes account of the uncertainty associated with the estimates of the random parameters and can provide exact measures of uncertainty. The maximum likelihood methods tend to overestimate precision because they ignore this uncertainty. In small samples this will be important especially when obtaining 'posterior' estimates for residuals. Bootstrap procedure is an alternative to take account of this uncertainty and will get approximate unbiased estimate. comparing to MCMC, bootstrap need less time and still much more than MLE methods. With bootstrap, we need define the repeat number and loop length based on the raw bootstrap results.

a.   Comparison of Estimation Methods and Hypothesis Tests for MGLMs

Each method has it own properties (as I summarized in Table II.2). MQL methods might result in severe underestimates, especially with small datasets[42]. Meanwhile, MQL1 is the most stable algorithm within quasi-likelihood methods. PQL methods are feasible and approach the true value based on some reports. PQL2 is more accurate than PQL1. The PQL methods have the shortcome of being unstable with poor convergence[49].

The Gaussian-Hermite numerical quadrature method is feasible in specific situations: it is feasible for a clustered model with one random effect; and can provide an approximate result with two random effect. We cannot apply numerical quadrature for a data randomized at the individual level or a model with more than two levels, or a random effect that does not follow a normal distribution. The Laplace method and numerical integration can provide better estimates than the MQL and PQL approxmiates. The Laplace, numerical integration, MCMC and Bootstrap methods perform well for all kinds of MGLMs, but they are computational intensive.

RIGLS PQL2 method, which provide a quick estimates, is ideal to explore the model. Otherwise, we need to choose Bootstrap, MCMC or the Laplace method to get accurate estimates and test the parameter. The choice of method depends on the convergence speed, availability of software, statistical efficiency, and obvious to obtain hypothesis test.

Table II.2: Comparison of Estimation Methods and Hypothesis Tests for MGLMs

Method	Bias	Time	Convergence	Hypothesis test		Software
				Fixed effect	Random effect	
MQL	Downward bias	Fast	Yes	T-test Wald test	Wald Test	MLwiN, R, Splus
PQL	Downward bias	Fast	Not Necessarily	T-test Wald test	Wald Test	MLwiN, SAS HLM, R, S
EM with Fisher Scoring	Bias	Fast	Not Necessarily	T-test Wald test Deviance test	Deviance test	HLM S
Gaussian Quadrature	Unbiased	Intensive	Yes	T-test, Wald Deviance test	Wald test Deviance test	SAS, aML Stata, MIXOR
Bootstrap	Approx. Unbiased	Intensive	Not Necessarily	T-test		MLwiN
				Quantile test		MLwiN
MCMC	Unbiased	Intensive	Yes	Quantile test BDIC		MLwiN WINBUGS

Approx: Approximate

MQL: Marginal quasi-likelihood estimate

PQL: Perpensity quasi-likelihood estimate

BDIC: Baysian deviance information criterion

EM: Expectation-Maximization

MCMC: Markov Chain Monte Carlo

E. EXPERIMENTAL DESIGN IN MULTILEVEL LOGISTIC MODELS

Less attention has been given to experimental design in the MLLMs than in the MLM. The main reason is the limitations of variables estimation methods for MLLMs. In these models, we must use iterative methods and cannot obtain analytical estimates except for the MQL1 method. Goldstein[25] reported that MQL1 method are downwardly biased and that simulation methods would be preferred to analytically biased estimation for comparing experimental designs in this setting.To date, only Zou[77] and Normand[52], and Moerbeek et al.[45][50] have reported simulation results on optimal experiment design for multilevel logistic models.

1. Zou and Normand's Sample Size Estimation in 2-level Logistic Models

In Bayesian theory, the multilevel logistic model can be written as a level-specific model:

$$\text{level 1}: Y_i|n, \theta_i \overset{\text{independent}}{\sim} \text{Binomial}(n_i, \theta_i) \tag{II.19}$$

At level 2, we can specify a prior distribution for θ_i:

$$\text{At level 2}: \theta_i|n, \alpha, \beta \overset{\text{i.i.d}}{\sim} \text{Beta}(\alpha, \beta) \tag{II.20}$$

At level 3, we can specify hyper-parameter distributions for α and β:

$$\text{level 3}: \alpha \sim \text{Gamma}(p_\alpha, q_\alpha) \quad \text{independent of} \quad \beta \sim \text{Gamma}(p_\beta, q_\beta) \tag{II.21}$$

The sample of clusters and right assumption of distribution of θ in (II.20) will affect the accuracy of the inference.

In 2001, Zou and Normand[52] used MCMC and MC simulation to get the central posterior interval when focusing on the level two parameter θ. At a 95% posterior confidence interval, we can decide the sample size of a cluster based on the balanced sample sizes for a 2-level logistic model. In 2002, Normand and Zou[52] expanded their 2001 research with a combined method of MCMC simulation and parametric approximation to get 95% posterior

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confidence interval for a 2\3 level balanced\unbalanced structure. Based on this, we can detect the sample size at the group level and individual level. Increasing the total sample size resulted in decreased width of the posterior confidence interval, whether the number of groups or the number or individuals was increased.

Their research is implemented in WINBUGS, the best known MCMC based Bayesian analysis package. Although WINBUGS is flexible enough to handle a very wide range of models, it is not as computationally efficient as other packages that can fit MCMC models, such as MlwiN[29]. A comparisan table[44] list the WINBUGS' computation time, 40-45 mins, for a two-level MLLM RI model. Therefore, the MCMC method is computationally intensive and not good for a large simulation study.

2. Moerbeek's Experimental Design in Multilevel Logistic Models without covariates

After comparing and applying numerical integration and quasi-Likelihood used(MQL1) for MLLMs, Moerbeek et al.[45] gives allocations of experimental units for optimal experimental design; specifically, the optimal level of randomization for the intervention with or without a fixed budget. She focuses on two kinds of two-level logistic models: the RI and RC logistic model without covariates. Optimality was defined in terms of the standard error of the intervention effect. In their method, the binary variable is coded as 1 and -1 for treatment and control group, which is called as "zero sum" coding.

a. Linearization and of the Two Level Logistic Model

As we discussed in Section II.D.1, the generalized 2-level model can be written in matrix style as shown below.

$$
\begin{aligned}
&y_{ij} = \pi_{ij} + (Z_\varepsilon \varepsilon)_{ij} = f(H) + (Z_\varepsilon \varepsilon)_{ij} = f((X\beta)_{ij} + (Z_\mu \mu)_j) + (Z_\varepsilon \varepsilon)_{ij}, \\
&\text{where } Z_{ij} = \sqrt{\pi_{ij}(1 - \pi_{ij})n_{ij}}, \ \sigma_\varepsilon^2 = 1, \ \mu_j \sim N(0, \sigma_{\nu_j}^2), \\
&\text{and } \pi_{ij} = f(H) = [1 + exp(-(X\beta + Z_\mu \mu))]^{-1}.
\end{aligned}
\tag{II.22}
$$

By applying the MQL1 method for π_{ij} at $(t+1)_{th}$ iteration in model II.22, we will get

$$
\begin{aligned}
\pi_{ij} = f(H_{t+1}) &\approx f(\tilde{H}_t) + (X_{ij}\beta + \mathbf{Z}_\mu\mu)f'(\tilde{H}_t) - X_{ij}\tilde{\beta}_t f'(\tilde{H}_t) \\
\pi_{ij}f'^{(-1)}(\tilde{H}_t) &= f(\tilde{H}_t)f'^{(-1)}(\tilde{H}_t) + X_{ij}\beta + \mathbf{Z}_\mu\mu - X_{ij}\tilde{\beta}_t.
\end{aligned} \tag{II.23}
$$

The next step is to write the standard 2-level logistic model (II.22) as

$$
y_{ij}f'^{(-1)}(\tilde{H}_t) = \pi_{ij}f'^{(-1)}(\tilde{H}_t) + (Z_\varepsilon\varepsilon)_{ij}f'^{(-1)}(\tilde{H}_t)
$$

and plug in (II.23) with some modification (detailed in Appendix D.A) to get a linearized 2-level logistic model(II.24).

$$
Y_{ij}^* = X_{ij}\beta + Z_\mu\mu + \varepsilon_{ij}^* \tag{II.24}
$$

where

$$
\begin{aligned}
y_{ij}^* &= (y_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + X_{ij}\tilde{\beta}_t \tag{II.25} \\
\varepsilon_{ij}^* &= (Z_\varepsilon\varepsilon)_{ij}f'^{(-1)}(\tilde{H}_t) = (Z_\varepsilon\varepsilon)_{ij} * [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1}. \tag{II.26}
\end{aligned}
$$

and

$$
\begin{aligned}
var(\varepsilon_{ij}^*) &= var(Z_\varepsilon\varepsilon_{ij} * [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1}) \\
&= [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} \\
&= [\frac{1}{1 + e^{-X\beta}}(1 - \frac{1}{1 + e^{-X\beta}})]^{-1} \\
&= 2 + e^{-X\beta} + e^{X\beta}, \tag{II.27}
\end{aligned}
$$

$$
E(\varepsilon_{ij}^*) = 0, \tag{II.28}
$$

$$
var(Y_{ij}^*) = Z_\mu' V_\mu Z_\mu + [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1}, \tag{II.29}
$$

$$
E(Y_{ij}^*) = X_{ij}\beta, \tag{II.30}
$$

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$$E(Y_{ij}) \approx (1 + e^{\frac{-X_{ij}\beta}{\sqrt{1+\sigma_\mu^2/1.7^2}}})^{-1} \tag{II.31}$$

$$\tag{II.32}$$

The generalized least squares estimator (GLS) of β_1 in the generalized linear mixed model[57] is

$$\hat{\beta} = (X'V^{-1}X)^{-1}X'V{-1}Y \tag{II.33}$$

Therefore, the GLS for the 2-level logistic model (detail in D) is shown as

$$\hat{\beta}_1 = \frac{\bar{y}^*_{..t} - \bar{y}^*_{..c}}{2} \tag{II.34}$$

By denoted δ^2 as

$$\hat{\beta}_1 = \frac{\bar{y}^*_t - \bar{y}^*_c}{2} \tag{II.35}$$

b.   Two Level RI Logistic Model

By using the MQL1 method, Moerbeek et al[45] derive the formula of $\widehat{\beta}_1$, $E(\widehat{\beta}_1)$, and $var(\widehat{\beta}_1)$, when randomizing at the individual and cluster levels. She derives the formulas for optimal allocation of units at each level with or without the budget and cost at each level. She also presents the formula for the $var(\widehat{\beta}_1)$, when the optimal sample size at each level and randomized level are given; the optimal randomization level is the individual level, which is consistent with her report on continuous outcomes. The optimal cluster size is 2 when the intervention is randomized at the individual level. When the randomization level is a cluster level, the optimal experimental design depends on the parameters. Moerbeek et al. summarized the variance formula in below table

For quasi-likelihood and numerical integration simulation methods, she simulates response variable through different combinations of assumed values of the allocation number at the two levels, β_0, β_1 and $\sigma_{\mu 0}^2$. The data set is simulated from one of 96 simulation combination of 1) sample size with and across sites(n=40, N=10; n=20, N=20; n=10, N=40), 2)assumed parameter estimates for β_0 (0), β_1 (1.5, 1, 0.5, 0), and $\sigma_{\mu 0}$ (1, 0.5, 0.25, 0). For each combination, 200 data sets were generated.

There are five steps in her simulation algorithm:

Table II.3: Estimated $\text{var}(\hat{\beta}_1)$ in 2-Level Logistic Model, Moerbeek et al[45]

Level of	$\text{var}(\hat{\beta}_1)$	
Randomization	RI Model	RC Model
Individual	$\frac{\delta^2}{nN}$	$\frac{\delta^2+n\sigma_{\mu_1}^2}{nN}$
Cluster	$\frac{\delta^2+n\sigma_{\mu_0}^2}{nN}$	$\frac{\delta^2+n(\sigma_{\mu_0}^2+\sigma_{\mu_1}^2)}{nN}$

note: X_{IJ} is in zero sum coding

note: n is assumed common cluster size

note: N is the number of cluster

note: δ^2 is level one residual $(var(e) = \sigma_e^2)$

where $\delta^2 = \frac{1}{2}(4 + e^{\beta_0+\beta_1} + e^{-\beta_0-\beta_1} + e^{\beta_0-\beta_1} + e^{-\beta_0+\beta_1})$

I. Select one of the above 96 combinations to simulate initial data.

II. Fit corresponded model using PQL to collect initial parameter estimates

III. Calculate the sample mean of β_1 $(\hat{\beta}_1)$.

IV. Calculate the sample variance $(var(\widehat{\beta}_1))$ by using sample mean variance in the 200 iterations.

V. Calculate correction factor$=\frac{\text{sample variance } var(\widehat{\beta}_1)}{\text{MQL1 analytic } var(\widehat{\beta}_1)}$

VI. Calculate the mean value of the correction factor.

VII. Calculate the mean value of the sample variance of $\widehat{\beta}_1$.

By comparing the correlation factor to 1, the optimal allocation in each design combination is obtained. They found that when the sample size is defined and β_1 is 0, $\text{var}(\widehat{\beta}_1)$ has a directly related to β_1, $\sigma_{\mu_0}^2$ and the sample size for individual level. For randomized at the group level, $\text{var}(\widehat{\beta}_1)$ is directly related only with β_1. Given the same data set combination, randomization at the group level has larger values of $\text{var}(\widehat{\beta}_1)$ than randomization at the individual level. When the sample size in the individual level and $\sigma_{\mu_0}^2$ are large, $\text{var}(\widehat{\beta}_1)$ will be large. The correction ratio for PQL1, PQL2, and numerical integration are the constants 1.1, 1.2 and 1.2, respectively. Then the design combination which obtain 1.1 will be the

best fit. Because the correction ratios are constant for PQL and numerical integration, they obtains the same conclusion of optimal design as the MQL1 method.

She reports that the MQL1 is downward biased for β_1, PQL1 is downward biased at most 10%, and PQL2 and numerical integration overestimate β_1 by about 5%. Comparing the $\text{var}(\sigma_{\mu0}^2)$, the PQL methods are unbiased and numerical integration is 2 times biased, and .5 to 1.5 times biased, when $\sigma_{\mu0}^2$ is equal to 0 and larger than 0, respectively.

c. Two level RC Logistic Models Moerbeek et al.[45] also give formulae of sample size and $var(\widehat{\beta}_1)$ (in Tabel II.3) varying by the randomization level. She reports the individual level is the optimal level of randomization. The optimal allocation for randomization on both the individual and group levels is parameter dependent. They found that the $var\widehat{\beta}_1$ in the RC logistic model was larger than that in the RI logistic model.

The numerical integration methods is easy to get a significantly higher estimate of variance when $\text{var}(\widehat{\beta}_1)$ is a small variance component. For both PQL methods and numerical integration, the $var(\widehat{\beta}_1)$ is directly related to $\sigma_{\mu1}^2$, β_1, and sample size in the individual level. MQL1 with a known variance component has the same results as PQL methods and numerical integration. The correct ratios, the ratio of true variance to sample mean simulation variance, are 1, 1,2, 1.4 for PQL1, PQL2, and numerical integration, respectively. Compared to the true value of $\beta1$, PQL1 underestimates by at most 10%, and PQL2 and numerical integration overestimate at most 5% .

3. Moerbeek's Experimental Design in Multilevel Logistic Models with Binary Covariate

Moerbeek et al.[50] discussed the sample size and optimal level of randomization for 2-level logistic models with binary covariate and with/out binary covariate interaction with intervention. She gives the formula of variance for intervention by MQL1 derivation and confirmed by PQL2 simulation. Based on the formula of variance for intervention, the optimal randomization level is the individual level.

1). Without Treatment and Covariate Interaction

In the 2-level linearized logistic model, the fixed effect is denoted in the matrix term, $X_{ij}\beta$. The 2-level linearized logistic model without the covariate are denoted the same as 2-level linearized logistic model with the covariate in the matrix form with different matrix elements. The variance formulae for the intervention ($\hat{\beta}_1$) and binary covariate ($\hat{\beta}_2$) in a 2-level logistic model without intervention and covariate interaction are summarized in Table II.4

Table II.4: Estimated $\mathrm{var}(\hat{\beta}_1)$ and $\mathrm{var}(\hat{\beta}_2)$ in 2-Level Logistic Model, Moerbeek et al[50]

Level of treatment	Level of covariate	$\mathrm{var}(\hat{\beta}_1)$	$\mathrm{var}(\hat{\beta}_2)$
Individual	Individual	$\frac{((\sigma_{--}^2+\sigma_{+-}^2)^{-1}+(\sigma_{-+}^2+\sigma_{++}^2)^{-1})^{-1}}{nN}$	$\frac{((\sigma_{--}^2+\sigma_{-+}^2)^{-1}+(\sigma_{+-}^2+\sigma_{++}^2)^{-1})^{-1}}{nN}$
Individual	Cluster	$\frac{((\sigma_{--}^2+\sigma_{+-}^2)^{-1}+(\sigma_{-+}^2+\sigma_{++}^2)^{-1})^{-1}}{nN}$	$\frac{(n\tau^2+(\sigma_{--}^2+\sigma_{-+}^2)^{-1}+(\sigma_{+-}^2+\sigma_{++}^2)^{-1})^{-1}}{nN}$
Cluster	Individual	$\frac{(n\tau_{\mu_0}^2+(\sigma_{--}^2+\sigma_{+-}^2)^{-1}+(\sigma_{-+}^2+\sigma_{++}^2)^{-1})^{-1}}{nN}$	$\frac{((\sigma_{--}^2+\sigma_{-+}^2)^{-1}+(\sigma_{+-}^2+\sigma_{++}^2)^{-1})^{-1}}{nN}$
Cluster	Cluster	$\frac{((\sigma_{--}^2+\sigma_{+-}^2+2n\tau^2)^{-1}+(\sigma_{-+}^2+\sigma_{++}^2+2n\tau^2)^{-1})^{-1}}{nN}$	$\frac{((\sigma_{--}^2+\sigma_{-+}^2+2n\tau^2)^{-1}+(\sigma_{+-}^2+\sigma_{++}^2+2n\tau^2)^{-1})^{-1}}{nN}$

note: β_1 and β_2 denote intervention and covariate

note: τ is variance in the cluster level

note: n is the same size in the cluster

note: N is the cluster number

$\{\hat{\pi}_{ij}(1-\hat{\pi}_{ij})\}^{-1}=\sigma_{ic}^2,$

In table II.3, σ_{ic}^2, the level one residual, refer to $\{\hat{\pi}_{ij}(1-\hat{\pi}_{ij})\}^{-1}$. The i and c in σ_{ic}^2 refer to intervention and covariate and take the sign of the value of intervention and covariate. For example, σ_{ic}^2 will be σ_{++}^2, if both intervention and covariate are coded as 1.

Assuming randomization at the individual level and or cluster, Moerbeek derives the variance of Y_{ij}^* using the MQL1 method and gives a table of variance for treatment and covariates. She claims that the optimal level is the individual level, no matter the location of the covariate and it is especially preferable when n and μ_j^2 are large. She confirms this analytic result using a PQL2 simulation. Within the simulation, there are five design factors: 1) allocation of units is defined as (n,N), which equals (20,80), (40,40), or (80,20); 2)$\sigma_{\mu_j}^2$ as .25, .5 or 1; 3) value of intercept as 0, 1, or 2; 4) estimate of intervention 0, .5, or 1; and

5) estimate of covariate as 0, .5, or 1. The author performs simulations of 1000 datasets for every combination($3^5 = 243$) of the above five design factors and fits models to these datasets using PQL2. She uses the sampling variance of parameters obtained from PQL2 divided by the variance derived from the MQL1 to get a correction factor. Comparing the variance among the parameters, she confirms her analytic results from the MQL1 that the optimal randomization level is the individual level.

2). With Treatment and Covariate Interaction

Similarly, she used MQl1 to derive the formula for the variance of interaction term, considering the intervention randomized at both the individual and cluster levels. She confirms her conclusion that the optimal randomization level is the individual level by simulation results, using PQL2.

In all of Moerbeek et al.'s work for balanced data , optimality was defined in terms of the standard error of the intervention effect. They discussed optimal allocation that minimized this standard error but did not specifically estimate power.

F.   FEIVESON'S METHOD TO SIMULATE POWER

Power is the probability that the null hypothesis will be rejected when it is false, given a specified alternative and type one error. A simulation method using a classic hypothesis test to estimate the power of complex models was outlined by Feiveson[15].

When the model is complex, the p value is an asymptotic approximation. Based on a specific experimental design, one can specify the overall sample size, and sample size at each level if a nested structure is applicable. The component of independent variables, distribution of the dependent variable, the α value and the statistical method are defined for a experiment. We will estimate the power with simulated data from the corresponding model using multiple replications of the experimental scenario and simply calculate the proportion of rejections as an estimate of the power.

The outline of Feiveson's algorithm is:

 I. Use the designated model to generate random outcome with
   - A specified experimental design and sample size
   - A value of X
   - A parameter value that defines as the distribution of Y.
 II. Run the designated model to generate random data.
III. Retrieve the p-value from the corresponding test statistics
IV. Repeat above steps a large number of times and save the p values for each iteration.
 V. Estimate the power as the proportion of observed p-values $\leq \alpha$ in across the iterations

Feiveson gives examples for t-tests, Possion regression, Cox regression, and rank sum tests. The author indicated that this approach could be used for multilevel data but he considered only single level data.

III. METHODS

In an observational study, the sample size is known. In the Volpp study, the sample size and racial distribution have been defined at each level. In this chapter, I extend the derivation of Moerbeek et al. [45] to allow for unbalance both between and within sites. I derive the analytic variance formulae for a fixed coefficient under unbalanced design in the two level RI and RC logistic models. I will outline the analysis of the Volpp data[34][76] and evaluate the analytic results by simulating outcome data based on the racial distributions in the Volpp data. I will then simulate the post-hoc power to detect the fixed effect of black race on the magnitude observed in this study. The variance of the race coefficient will be derived using alternative parameterization of race, under several selected balanced and unbalanced design scenarios (detailed in Appendix D.B).

A.   DESIGN AND PARAMETERIZATION

1.   Design Scenarios Considered

In this dissertation, I restricted my attention to a two-level logistic model. Because of hierarchical data structure, the unbalanced design is complicated. Unbalanced design might occur within and/or across sites. For instance, when we have the same sample size for each site(n), we might see the same proportion of black patients (w) or a site-specific proportion (w_j). Alternatively, we might have site specific sample sizes (n_j) with either the same or a site-specific proportion of black patients within each site. In Table III.1, I describe the notation for all the possible balanced and unbalanced design scenarios for the 2-level logistic

model. Within this table, w_j refers to the proportion of black patients at the j_{th} site; w refers to an assumed common race proportion across sites; n_j refers to the total sample size for the j_{th} site; n refers to an assumed common sample size across sites; B_* refers to the design scenarios with the same sample size per site; U_* refers to the design scenarios with a site specific sample size; * indicates $\frac{1}{2}$ for a balanced design within sites, w denotes an assumed common site proportion, and w_j denotes a for site-specific proportion of black patients.

Table III.1: Unbalanced Design Scenarios in a 2-level Model

			Across Sites	
			Balance	Imbalance
	Balance	$w_j = \frac{1}{2}$	$B_{\frac{1}{2}}$	$U_{\frac{1}{2}}$
Within Sites	Imbalance	$w_j = w \neq \frac{1}{2}$	B_w	U_w
		w_j	B_j	U_j

2. Parameterization of Race

As we shown in Chapter 2, the generalized 2-level model can be written in matrix style as model II.7

The Volpp study focuses on comparing 30 day mortality between white and black patients within sites. Race, as a binary variable in the model, can be coded either as 1 and -1 ("Sum to Zero" constraints), or as 1 and 0 ("Reference level" constraints), for black and white patients, respectively. In Moerbeek's work, 1 and -1 coding was used, which follows MIXOR's coding. I will use 1 and 0 coding in this dissertation, because MLwiN uses 1 and 0 coding and I will use MLwiN to implement the simulation. Different codings of race yields different parameter estimates with different interpretations. The parameter estimate of the black race coefficient obtained using 0 and 1 coding will be twice that value of the corresponding parameter obtained using the 1 and -1 coding. For interpretation, the main difference for the race-specific mortality is that the reference level coding gives the black odds ratio(OR) directly (relative to white patients). The sum to zero coding gives parameters that require a linear transformation of to provide comparable ORs.

a. Sum to Zero Constraints

We can write the 2-level RI models (III.1). β_0 is the intercept term, which represents the mean mortality in the population. β_1 is the parameter estimate of black race. e^{β_1}, the OR of a black patient, represents the odds of black mortality to average mortality of pneumonia patients at that site. x_{ij} is coded as 1 for black patients and -1 for white patients. ε_{ij} is the level 1 residual.

$$logit\pi_{ij} = \beta_0 + \beta_1 x_{ij} + \mu_{0j} + \varepsilon_{ij} \tag{III.1}$$

The race-specific models will be (III.2) and (III.3) for blacks and whites.

$$\text{Black only} \qquad logit\pi_{ij} = \beta_0 + \beta_1 + \mu_{0j} + \varepsilon_{ij} \tag{III.2}$$

$$\text{White only} \qquad logit\pi_{ij} = \beta_0 - \beta_1 + \mu_{0j} + \varepsilon_{ij} \tag{III.3}$$

Comparing (III.2) and (III.3), the odds of mortality for a black patient relative to a white patient at same site is $e^{2\beta}$, for the sum to zero parameterization.

We can write the random coefficient model as III.4. In this equation, μ_{0j} is the level 2 residual, which represents the variation within the j_{th} site. μ_{1j} is the level 2 variance of black race(x_{ij}), which represent the black race and site interaction.

$$logit\pi_{ij} = \beta_0 + \beta_1 x_{ij} + \mu_{0j} + \mu_{1j} x_{ij} + \varepsilon_{ij} \tag{III.4}$$

The race specific models for the RC model will be (III.32) and (III.33) for blacks and whites, respectively.

$$\text{Black only} \qquad logit\pi_{ij} = \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ij} \tag{III.5}$$

$$\text{White only} \qquad logit\pi_{ij} = \beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \varepsilon_{ij} \tag{III.6}$$

b. Reference level Constraints

When we code black patients as $x_{ij} = 1$ and white patients as $x_{ij} = 0$ for β_1, the model will the same as III.1, except that the intepretation of β_1 is different. The race specific models can be written as in equation (III.7) and (III.8) for black and white patients, respectively.

$$\text{Black only} \qquad logit\pi_{ij} = \beta_0 + \beta_1 + \mu_{0j} + \varepsilon_{ij} \qquad \text{(III.7)}$$

$$\text{White only} \qquad logit\pi_{ij} = \beta_0 + \mu_{0j} + \varepsilon_{ij} \qquad \text{(III.8)}$$

The race specific RC models will be (III.9) and (III.10) for black and white patients, respectively.

$$\text{Black only} \qquad logit\pi_{ij} = \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ij} \qquad \text{(III.9)}$$

$$\text{White only} \qquad logit\pi_{ij} = \beta_0 + \mu_{0j} + \varepsilon_{ij} \qquad \text{(III.10)}$$

In the above four models, β_0 is the intercept term, which represents the average mortality for white veterans; β_1 is the parameter estimate of race; e^{β_1} is the OR of 30 day mortality for black patients relative to white patients at the same site. Both ε_{ij} and μ_{0j} have the same interpretation as in the sum to zero parameterization.

B.   VARIANCE DERIVATION

We usually write RI and RC logistic models as in (III.1) and (III.4). If the outcome variable is not normal and the error term is assumed to be normal, linearization is required for the 2-level logistic model to transform these two components into approximately normal distributed variable. Quasi-likelihood estimation can be applied to the linearized model to obtain the variance of fixed effects. As shown in Chapter (in Section II.D.2.a), MQL1 assumes that estimate of the random effect from previous iteration is 0. This avoids complicated calculations related to the random parts, which simplifies the derivation of the variance of fixed effects.

1.   Variance of the Black Coefficient Under Sum to Zero Constraints

a.   RI Model

By applying the linearized 2-level logistic model from (II.24) to the RI model (III.1), the linearized 2-level RI model can be written as

$$\mathbf{y}_{ij}^* = \beta_0 + \beta_1 x_{ij} + \mu_{0j} + \varepsilon_{ij}^* \tag{III.11}$$

Therefore, the race specific models will be (III.12) and (III.13) for black patients and white patients, respectively.

$$\mathbf{y}_{ij}^* = \beta_0 + \beta_1 + \mu_{0j} + \varepsilon_{ij}^* \qquad \text{Black} \tag{III.12}$$

$$\mathbf{y}_{ij}^* = \beta_0 - \beta_1 + \mu_{0j} + \varepsilon_{ij}^* \qquad \text{White} \tag{III.13}$$

From now on, any subscripts in the mathematics notation will follow below notation. "." is refers to any number in $i_t h$ individual or (j_{th} cluster); B refers to black patients; and W refers to white patients. .

The average mortality for black patients ($\widehat{Y}_{..B}^*$) in the RI model will be

$$\bar{y}_{..B}^* = \beta_0 + \beta_1 + \bar{\varepsilon}_{..B}^* \tag{III.14}$$

The average mortality for white patients in the RI model will be

$$\bar{y}^*_{..W} = \beta_0 - \beta_1 + \bar{\varepsilon}^*_{..W}. \tag{III.15}$$

Consequently, I get a GLS estimates of $\widehat{\beta}_1$ (detailed in Appendix D.C) as

$$
\begin{aligned}
\widehat{\beta}_1 &= \frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2} \\
&= \frac{\sum_{j=1}^N \frac{\sum_{i=1}^{n_{jB}} \varepsilon^*_{ijB}}{n_{jB}} - \sum_{j=1}^N \frac{\sum_{i=1}^{n_{jw}} \varepsilon^*_{ijW}}{n_{jW}}}{2N} \\
&= \frac{\bar{\varepsilon}^*_{..B} - \bar{\varepsilon}^*_{..W}}{2} \tag{III.16}
\end{aligned}
$$

By following Moerbeek's notation, I denoted the estimated variance as $var(\hat{\beta}_1)$. The estimated variance of $\widehat{\beta}_1$ is

$$
\begin{aligned}
var(\hat{\beta}_1) &= var(\frac{\bar{\varepsilon}^*_{..B} - \bar{\varepsilon}^*_{..W}}{2}) \\
&= \frac{\frac{(\sum_{j=1}^N n_{jB})\sigma^{2*}_{\varepsilon_{ijB}}}{(\sum_{j=1}^N n_{jB})^2} + \frac{(\sum_{j=1}^N n_{jW})\sigma^{2*}_{\varepsilon_{ijW}}}{(\sum_{j=1}^N n_{jW})^2}}{4} \\
var(\hat{\beta}_1) &= \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^N n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^N n_{jW}}}{4} \tag{III.17}
\end{aligned}
$$

By applying (II.27), the race specific variance of residuals are (III.19) and (III.18) for black and white patients, respectively.

$$\mathbf{var}(\varepsilon^*_{\mathbf{ijB}}) = 2 + e^{-(\beta_0 + \beta_1)} + e^{(\beta_0 + \beta_1)} \qquad \text{Black} \tag{III.18}$$

$$\mathbf{var}(\varepsilon^*_{\mathbf{ijW}}) = 2 + e^{-(\beta_0 - \beta_1)} + e^{(\beta_0 - \beta_1)} \qquad \text{White} \tag{III.19}$$

For condition $B_{\frac{1}{2}}$: When the experimental design is balanced both across sites and within sites, the sample size for each site is $\sum_{j=1}^N n_{ijB} = \sum_{j=1}^N n_{ijW} = \frac{M}{2}$. As a result, the variance of the fixed coefficient of black race is

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\frac{M}{2}} + \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\frac{M}{2}}}{4} \\
var(\hat{\beta}_1) &= \frac{\frac{1}{2}(\sigma^{2*}_{\varepsilon_{ijB}} + \sigma^{2*}_{\varepsilon_{ijW}})}{M}
\end{aligned}
$$

$$\tag{III.20}$$

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Following Moerbeek's notation on δ^2 (as shown in Table II.3), the variance can be written as $var(\beta_1) = \frac{\delta^2}{M}$.

For condition $B_{\bar{w}}$: The sample size is the same across the sites, i.e. $n_1 = n_2 = \cdots = n_j = n$ and the site specific black proportion(as site-specific weight, w_j) is the same across site, ie. $w_j = \bar{w} \neq \frac{1}{2}$. The race specific total population number is

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \sum_{j=1}^{N} w_j n_j = \sum_{j=1}^{N} \bar{w} n = \bar{w} n N = \bar{w} M \\
\sum_{j=1}^{N} n_{jW} &= \sum_{j=1}^{N} (1 - w_j) n_j = \sum_{j=1}^{N} (1 - \bar{w}) n = (1 - \bar{w}) n N = (1 - \bar{w}) M. \quad \text{(III.21)}
\end{aligned}
$$

Therefore, the variance of the fixed coefficient for black race is

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
&= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\bar{w} M} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{(1 - \bar{w}) M}}{4} \\
&= \frac{(1 - \bar{w}) \sigma_{\varepsilon_{ijB}}^{2*} + \bar{w} \sigma_{\varepsilon_{ijW}}^{2*}}{4 \bar{w} (1 - \bar{w}) M} \quad \text{(III.22)}
\end{aligned}
$$

For condition B_{w_j}: In this scenario, I assume the same sample size across sites ($n_1 = n_2 = \cdots = n_j = n$), but a site specific weight is $w_j = w_j$ for j_{th} site. The race specific total population number is

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \sum_{j=1}^{N} w_j n_j = n \sum_{j=1}^{N} w_j \quad \text{and} \\
\sum_{j=1}^{N} n_{jW} &= \sum_{j=1}^{N} (1 - w_j) n_j = n \sum_{j=1}^{N} (1 - w_j). \quad \text{(III.23)}
\end{aligned}
$$

for black and white patients, respectively. The variance of the fixed coefficient for black race is

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
&= \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{n \sum_{j=1}^{N} w_j} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{n \sum_{j=1}^{N} (1-w_j)}}{4} \\
&= \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{n \sum_{j=1}^{N} w_j} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{n(N-\sum_{j=1}^{N} w_j)}}{4} \\
&= \frac{(N - \sum_{j=1}^{N} w_j)\sigma^{2*}_{\varepsilon_{ijB}} + \sum_{j=1}^{N} w_j \sigma^{2*}_{\varepsilon_{ijW}}}{4n(N - \sum_{j=1}^{N} w_j)\sum_{j=1}^{N} w_j}
\end{aligned}
\tag{III.24}
$$

When the sample sizes are the same across sites, the variance of the fixed coefficient for black race in the RI model are summarized in Table III.2.

Table III.2: Var(Black) in the RI model with Equal Sample Size Across N Sites, and Different Sample Sizes within Sites and Sum to Zero Coding for Race

Weight(w_j)	Var(Black)
$\frac{1}{2}$	$\frac{\frac{1}{2}(\sigma^{2*}_{\varepsilon_{ijB}}+\sigma^{2*}_{\varepsilon_{ijW}})}{M}$
$\bar{w} \neq \frac{1}{2}$	$\frac{(1-\bar{w})\sigma^{2*}_{\varepsilon_{ijB}}+\bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{4\bar{w}(1-\bar{w})M}$
w_j	$\frac{(N-\sum_{j=1}^{N} w_j)\sigma^{2*}_{\varepsilon_{ijB}}+\sum_{j=1}^{N} w_j \sigma^{2*}_{\varepsilon_{ijW}}}{4n(N-\sum_{j=1}^{N} w_j)\sum_{j=1}^{N} w_j}$

Note: $\sigma^{2*}_{\varepsilon_{ijB}} = 2 + e^{-(\beta_0+\beta_1)} + e^{(\beta_0+\beta_1)}$

and $\sigma^{2*}_{\varepsilon_{ijW}} = 2 + e^{-(\beta_0-\beta_1)} + e^{(\beta_0-\beta_1)}$

M is total sample size

For condition $U_{\frac{1}{2}}$: In this scenario, I assume unequal site specific sample sizes ($n_1 \neq n_2 \neq \cdots \neq n_j$, not necessarily all unequal) with the same proportions of black and white patients

at each site. The j_{th} site sample size is $n_{jB} = n_{jW} = \frac{n_j}{2}$, nd the race specific sample sizes are

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \sum_{j=1}^{N} \frac{1}{2} n_j = \frac{1}{2} \sum_{j=1}^{N} n_j = \frac{M}{2} \qquad \text{black, and} \\
\sum_{j=1}^{N} n_{jW} &= \sum_{j=1}^{N} \frac{1}{2} n_j = \frac{1}{2} \sum_{j=1}^{N} n_j = \frac{M}{2} \qquad \text{white.}
\end{aligned}
$$

(III.25)

As a result, the formula in (III.17) can be written as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
var(\hat{\beta}_1) &= \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\frac{M}{2}} + \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\frac{M}{2}}}{4}
\end{aligned}
$$

(III.26)

For condition $U_{\bar{w}}$: In this scenario, sample size vary by site ($n_1 \neq n_2 \neq \cdots \neq n_j$, not necessarily all unequal) with the same proportion of black patients at each site ($w_j = \bar{w}$). The race specific populations are

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \sum_{j=1}^{N} \bar{w} n_j = \bar{w} \sum_{j=1}^{N} n_j = \bar{w} M \qquad \text{and} \\
\sum_{j=1}^{N} n_{jW} &= \sum_{j=1}^{N} (1 - \bar{w}) n_j = (1 - \bar{w}) \sum_{j=1}^{N} n_j = (1 - \bar{w}) M
\end{aligned}
$$

(III.27)

for black and white patients, respectively. As a result, the variance of the fixed coefficient of black race is

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
&= \frac{(1 - \bar{w}) \sigma^{2*}_{\varepsilon_{ijB}} + \bar{w} \sigma^{2*}_{\varepsilon_{ijW}}}{4 \bar{w} (1 - \bar{w}) M}
\end{aligned}
$$

(III.28)

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For condition U_j: The site specific sample size is $n_1 \neq n_2 \neq \cdots \neq n_j$ (not necessarily all unequal) and the site specific weights vary (w_j). The site-specific populations are

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \sum_{j=1}^{N} w_j n_j \qquad \text{and} \\
\sum_{j=1}^{N} n_{jW} &= \sum_{j=1}^{N} (1 - w_j) n_j,
\end{aligned} \tag{III.29}
$$

for black and white patient, respectively. Variance will be derived as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\dfrac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \dfrac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}}}{4} \\[2mm]
&= \frac{\dfrac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} w_j n_j} + \dfrac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} (1-w_j) n_j}}{4} \\[2mm]
&= \frac{\dfrac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} w_j n_j} + \dfrac{\sigma_{\varepsilon_{ijW}}^{2*}}{(\sum_{j=1}^{N} n_j - \sum_{j=1}^{N} w_j n_j)}}{4} \\[2mm]
&= \frac{\dfrac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} w_j n_j} + \dfrac{\sigma_{\varepsilon_{ijW}}^{2*}}{M - \sum_{j=1}^{N} w_j n_j}}{4} \\[2mm]
&= \frac{(M - \sum_{j=1}^{N} w_j n_j)\sigma_{\varepsilon_{ijB}}^{2*} + (\sum_{j=1}^{N} w_j n_j)\sigma_{\varepsilon_{ijW}}^{2*}}{4(M - \sum_{j=1}^{N} w_j n_j)\sum_{j=1}^{N} w_j n_j}.
\end{aligned} \tag{III.30}
$$

Consequently, I have a site specific sample size under different weight scenarios, I can calculate the variance of race in the RI model as shown in Table III.3.

b.   RC Model   In the RC model, the linearized model can be written as (III.31)

$$
\mathbf{Y}_{ij}^* = \beta_0 + \beta_1 x_{ij} + \mu_{0j} + \mu_{1j} x_{ij} + \varepsilon_{ij}^*. \tag{III.31}
$$

The race specific RC models will be (III.32) and (III.33) for black and white patients, respectively.

$$
\mathbf{Y}_{ij}^* = \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ij}^* \tag{III.32}
$$

$$
\mathbf{Y}_{ij}^* = \beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \varepsilon_{ij}^* \tag{III.33}
$$

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Table III.3: Var(Black) in the RI model with Unequal Sample Sizes Across Sites, and Sum to Zero Coding for Race

Weight(w_j)	Var(Black)
$\frac{1}{2}$	$\dfrac{\frac{1}{2}(\sigma^{2*}_{\varepsilon_{ijB}}+\sigma^{2*}_{\varepsilon_{ijW}})}{M}$
$\bar{w} \neq \frac{1}{2}$	$\dfrac{(1-\bar{w})\sigma^{2*}_{\varepsilon_{ijB}}+\bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{4\bar{w}(1-\bar{w})M}$
w_j	$\dfrac{(M-\sum_{j=1}^{N} w_j n_j)\sigma^{2*}_{\varepsilon_{ijB}}+(\sum_{j=1}^{N} w_j n_j)\sigma^{2*}_{\varepsilon_{ijW}}}{4(M-\sum_{j=1}^{N} w_j n_j)\sum_{j=1}^{N} w_j n_j}$

Note: $\quad \sigma^{2*}_{\varepsilon_{ijB}} = 2 + e^{-(\beta_0+\beta_1)} + e^{(\beta_0+\beta_1)}$

and $\quad \sigma^{2*}_{\varepsilon_{ijW}} = 2 + e^{-(\beta_0-\beta_1)} + e^{(\beta_0-\beta_1)}$

M is total sample size

Consequently,

$$\mathbf{Y}^*_{..B} = \beta_0 + \beta_1 + \varepsilon^*_{..B} \qquad \text{black} \tag{III.34}$$

$$\mathbf{Y}^*_{..W} = \beta_0 - \beta_1 + \varepsilon^*_{..W} \qquad \text{white} \tag{III.35}$$

The GLS estimate of $\widehat{\beta}_1$ is

$$
\begin{aligned}
\widehat{\beta}_1 &= \frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2} \\
&= \frac{\sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} y^*_{ijB}}{n_{jB}} - \sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} y^*_{ijW}}{n_{jW}}}{2N} \\
&= \frac{\bar{\bar{\varepsilon}}^*_{..B} - \bar{\bar{\varepsilon}}^*_{..W}}{2} + \bar{\mu}_{1j} \\
&= \frac{\sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} \varepsilon^*_{..B}}{n_{jB}} - \sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} \varepsilon^*_{..W}}{n_{jW}}}{2N} + \bar{\mu}_{1j}
\end{aligned}
\tag{III.36}
$$

The variance of $\widehat{\beta_1}$ is

$$
\begin{aligned}
var(\hat{\beta}_1) = \ &= \ var(\frac{\beta_0 + \beta_1 + \bar{\varepsilon}^*_{..B} - (\beta_0 - \beta_1 + \bar{\varepsilon}^*_{..W})}{2}) + var(\bar{\mu}_{1j}) \\
&= \ \frac{\frac{(\sum_{j=1}^{N} n_{jB})\sigma^{2*}_{\varepsilon_{ijB}}}{(\sum_{j=1}^{N} n_{jB})^2} + \frac{(\sum_{j=1}^{N} n_{jW})\sigma^{2*}_{\varepsilon_{ijW}}}{(\sum_{j=1}^{N} n_{jW})^2}}{4} + \frac{\sigma^2_{\mu_1}}{N} \\
var(\hat{\beta}_1) \ &= \ \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} n_{jW}}}{4} + \frac{\sigma^2_{\mu_1}}{N}
\end{aligned}
$$

(III.37)

By comparing the variance formula in the RI model (III.17) to the RC model (III.37), the only difference is the additional term $\frac{\sigma^2_{\mu_1}}{N}$, the level two residual term. As a result, when I have the same sample size across sites, the variance of the fixed coefficient of black race in the RC model is summarized in Table III.4 under different weight scenarios.

Table III.4: Var(Black) in the RC model with Equal Sample Sizes Across N Sites, and Different Sample Sizes within Sites and Sum to Zero Coding for Race

Weight(w_j)	Var(Black)
$\frac{1}{2}$	$\frac{\frac{1}{2}(\sigma^{2*}_{\varepsilon_{ijB}} + \sigma^{2*}_{\varepsilon_{ijW}})}{M} + \frac{\sigma^2_{\mu_1}}{N}$
$\bar{w} \neq \frac{1}{2}$	$\frac{(1-\bar{w})\sigma^{2*}_{\varepsilon_{ijB}} + \bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{4\bar{w}(1-\bar{w})M} + \frac{\sigma^2_{\mu_1}}{N}$
w_j	$\frac{(N-\sum_{j=1}^{N} w_j)\sigma^{2*}_{\varepsilon_{ijB}} + \sum_{j=1}^{N} w_j\sigma^{2*}_{\varepsilon_{ijW}}}{4n(N-\sum_{j=1}^{N} w_j)\sum_{j=1}^{N} w_j} + \frac{\sigma^2_{\mu_1}}{N}$

Note: $\sigma^{2*}_{\varepsilon_{ijB}} = 2 + e^{-(\beta_0+\beta_1)} + e^{(\beta_0+\beta_1)}$

and $\sigma^{2*}_{\varepsilon_{ijW}} = 2 + e^{-(\beta_0-\beta_1)} + e^{(\beta_0-\beta_1)}$

M is total sample size

The corresponding variance for the RC logistic model are shown in Table III.5in, when the sample sizes vary by site.

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Table III.5: Var(Black) in the RC model with Unequal Sample Sizes Across Sites and Sum to Zero Coding for Race

Weight(w_j)	Var(Black)
$\frac{1}{2}$	$\frac{\frac{1}{2}(\sigma^{2*}_{\varepsilon_{ijB}}+\sigma^{2*}_{\varepsilon_{ijW}})}{M} + \frac{\sigma^2_{\mu_1}}{N}$
$\bar{w} \neq \frac{1}{2}$	$\frac{(1-\bar{w})\sigma^{2*}_{\varepsilon_{ijB}}+\bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{4\bar{w}(1-\bar{w})M} + \frac{\sigma^2_{\mu_1}}{N}$
w_j	$\frac{(M-\sum_{j=1}^{N} w_j n_j)\sigma^{2*}_{\varepsilon_{ijB}}+(\sum_{j=1}^{N} w_j n_j)\sigma^{2*}_{\varepsilon_{ijW}}}{4(M-\sum_{j=1}^{N} w_j n_j)\sum_{j=1}^{N} w_j n_j} + \frac{\sigma^2_{\mu_1}}{N}$

Note: $\sigma^{2*}_{\varepsilon_{ijB}} = 2 + e^{-(\beta_0+\beta_1)} + e^{(\beta_0+\beta_1)}$

and $\sigma^{2*}_{\varepsilon_{ijW}} = 2 + e^{-(\beta_0-\beta_1)} + e^{(\beta_0-\beta_1)}$

M is total sample size

2. Variance of the Fixed Efficient of Black Race Under Reference Level Coding

a. RI Model

The linearized RI models are shown to be the same under both sum to zero and reference level parameterizations of race with different statistics interpretations. The linearized RI model for black is the same as (III.12), because blacks are coded as 1 in both. The linearized RI model for whites can be written as

$$y^*_{ij} = \beta_0 + \mu_{0j} + \varepsilon^*_{ij} \tag{III.38}$$

The average mortality for blacks in the RI model is

$$y^*_{..B} = \beta_0 + \beta_1 + \varepsilon^*_{..B} \tag{III.39}$$

and the average mortality for whites in the RI model is

$$y^*_{..W} = \beta_0 + \varepsilon^*_{..W} \tag{III.40}$$

Therefore, the GLS estimate of $\widehat{\beta}_1$ is

$$
\begin{aligned}
\widehat{\beta}_1 &= \bar{y}^*_{..B} - \bar{y}^*_{..W} \\
&= \frac{\sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} \varepsilon^*_{ijB}}{n_{jB}} - \sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jW}} \varepsilon^*_{ijW}}{n_{jW}}}{N}
\end{aligned} \tag{III.41}
$$

The $\widehat{\beta}_1$ in reference level coding is double the value of $\widehat{\beta}_1$ in the sum to zero coding. For the reference level coding, the variance in each design scenario is four times the value of the corresponding variance in the sum to zero coding. When I have same sample size across sites under different weight scenarios, we can calculate the variance of race in the RI model as shown in Table III.6.

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Table III.6: Var(Black) in the RI model with Equal Sample Sizes Across N Sites and Different Patterns of Sample Sizes within Site, Under Reference Level Coding for Race

Weight (w_j)	Var(Black)
$\frac{1}{2}$	$\frac{2(\sigma^{2*}_{\varepsilon_{ijB}}+\sigma^{2*}_{\varepsilon_{ijW}})}{M}$
$\bar{w} \neq \frac{1}{2}$	$\frac{(1-\bar{w})\sigma^{2*}_{\varepsilon_{ijB}}+\bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{\bar{w}(1-\bar{w})M}$
w_j	$\frac{(N-\sum_{j=1}^{N}w_j)\sigma^{2*}_{\varepsilon_{ijB}}+\sum_{j=1}^{N}w_j\sigma^{2*}_{\varepsilon_{ijW}}}{n(N-\sum_{j=1}^{N}w_j)\sum_{j=1}^{N}w_j}$

Note: $\sigma^{2*}_{\varepsilon_{ijB}} = 2 + e^{-(\beta_0+\beta_1)} + e^{(\beta_0+\beta_1)}$

and $\sigma^{2*}_{\varepsilon_{ijW}} = 2 + e^{-(\beta_0-\beta_1)} + e^{(\beta_0-\beta_1)}$

M is total sample size

b.   RC Model

The linearized RC models are the same under both race codings. The black linearized RC model is the same as (III.32), because blacks are coded as 1 in both codings. The linearized RC model for whites can be written as (III.34)

$$\mathbf{Y}^*_{ij} = \beta_0 + \mu_{0j} + \varepsilon^*_{ij}. \tag{III.42}$$

The average mortality for blacks in the RI model will be

$$\mathbf{Y}^*_{..B} = \beta_0 + \beta_1 + \varepsilon^*_{..B}. \tag{III.43}$$

Similarly, the average mortality for white patients in the RI model will be

$$\mathbf{Y}^*_{..W} = \beta_0 + \varepsilon^*_{..W}. \tag{III.44}$$

Therefore, the GLS estimate of $\widehat{\beta}_1$ is

$$\begin{aligned} \widehat{\beta}_1 &= \bar{y}^*_{..B} - \bar{y}^*_{..W} \\ &= \frac{\sum_{j=1}^{N}\frac{\sum_{i=1}^{n_{jB}}\varepsilon^*_{ijB}}{n_{jB}} - \sum_{j=1}^{N}\frac{\sum_{i=1}^{n_{jB}}\varepsilon^*_{ijW}}{n_{jW}}}{N} + \bar{\mu}_{1j} \end{aligned} \tag{III.45}$$

Table III.7: Var(Black) In the RI model with Unequal Sample Sizes Across Sites, Under Reference Level Coding for Race

Weight (w_j)	Var(Black)
$\frac{1}{2}$	$\frac{2(\sigma^{2*}_{\varepsilon_{ijB}}+\sigma^{2*}_{\varepsilon_{ijW}})}{M}$
$\bar{w} \neq \frac{1}{2}$	$\frac{(1-\bar{w})\sigma^{2*}_{\varepsilon_{ijB}}+\bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{\bar{w}(1-\bar{w})M}$
w_j	$\frac{(M-\sum_{j=1}^{N} w_j n_j)\sigma^{2*}_{\varepsilon_{ijB}}+(\sum_{j=1}^{N} w_j n_j)\sigma^{2*}_{\varepsilon_{ijW}}}{(M-\sum_{j=1}^{N} w_j n_j)\sum_{j=1}^{N} w_j n_j}$

Note: $\sigma^{2*}_{\varepsilon_{ijB}} = 2 + e^{-(\beta_0+\beta_1)} + e^{(\beta_0+\beta_1)}$

and $\sigma^{2*}_{\varepsilon_{ijW}} = 2 + e^{-(\beta_0-\beta_1)} + e^{(\beta_0-\beta_1)}$

M is total sample size

The $\widehat{\beta_1}$ in reference level coding is double the value of the sum to zero coding. The variance in each design scenario will be four times the value of the related variance in sum to zero coding. The design scenario specific variances of the race coefficient are summarized as follows. When I have the same sample size across sites under different weight scenarios, I can calculate the variance of race in the RC model as shown in Table III.8. When I have a site specific sample size under different weight scenarios, I can calculate the variance of race in the RC model as shown in Table III.9.

The variance under reference level constraints is illustrated to the Volpp study to obtain the analytic variance. A ratio of analytic variance to the empirical variance is used to evaluate the analytic formulae.

Table III.8: Var(Black) in the RC model with Equal Sample Sizes Across N Sites and Different Patterns of Sample Sizes within Site , Under Reference Level Coding for Race

Weight (w_j)	Var(Black)
$\frac{1}{2}$	$\frac{2(\sigma^{2*}_{\varepsilon_{ijB}}+\sigma^{2*}_{\varepsilon_{ijW}})}{M} + \frac{\sigma^2_{\mu_1}}{N}$
$\bar{w} \neq \frac{1}{2}$	$\frac{(1-\bar{w})\sigma^{2*}_{\varepsilon_{ijB}}+\bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{\bar{w}(1-\bar{w})M} + \frac{\sigma^2_{\mu_1}}{N}$
w_j	$\frac{(N-\sum_{j=1}^{N} w_j)\sigma^{2*}_{\varepsilon_{ijB}}+\sum_{j=1}^{N} w_j\sigma^{2*}_{\varepsilon_{ijW}}}{n(N-\sum_{j=1}^{N} w_j)\sum_{j=1}^{N} w_j} + \frac{\sigma^2_{\mu_1}}{N}$

Note: $\sigma^{2*}_{\varepsilon_{ijB}} = 2 + e^{-(\beta_0+\beta_1)} + e^{(\beta_0+\beta_1)}$

and $\sigma^{2*}_{\varepsilon_{ijW}} = 2 + e^{-(\beta_0-\beta_1)} + e^{(\beta_0-\beta_1)}$

M is total sample size

Table III.9: Var(Black) In the RC model with Unequal Sample Sizes Across Sites, Under Reference Level Coding for Black

Weight (w_j)	Var(Black)
$\frac{1}{2}$	$\frac{2(\sigma^{2*}_{\varepsilon_{ijB}}+\sigma^{2*}_{\varepsilon_{ijW}})}{M} + \frac{\sigma^2_{\mu_1}}{N}$
$\bar{w} \neq \frac{1}{2}$	$\frac{(1-\bar{w})\sigma^{2*}_{\varepsilon_{ijB}}+\bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{\bar{w}(1-\bar{w})M} + \frac{\sigma^2_{\mu_1}}{N}$
w_j	$\frac{(M-\sum_{j=1}^{N} w_jn_j)\sigma^{2*}_{\varepsilon_{ijB}}+(\sum_{j=1}^{N} w_jn_j)\sigma^{2*}_{\varepsilon_{ijW}}}{(M-\sum_{j=1}^{N} w_jn_j)\sum_{j=1}^{N} w_jn_j} + \frac{\sigma^2_{\mu_1}}{N}$

Note: $\sigma^{2*}_{\varepsilon_{ijB}} = 2 + e^{-(\beta_0+\beta_1)} + e^{(\beta_0+\beta_1)}$

and $\sigma^{2*}_{\varepsilon_{ijW}} = 2 + e^{-(\beta_0-\beta_1)} + e^{(\beta_0-\beta_1)}$

M is total sample size

C.   SUBSAMPLE SELECTION

The causes of racial disparities are not well understood. It may be that black and white veterans may receive care at different VA sites; those sites that care disproportionately for blacks may differ in terms of quality of care or clinical outcomes from other sites. The objective in Jha's study [34] was to determine the concentration of hospital care for black veterans, the variability of outcomes overall and in terms of black/white differences, and the degrees to which observed differences in mortality rates of blacks and whites vary in accordance with the proportion of blacks treated.

To assess the impact of excluding states with relatively few black patients, I will define a subsample of sites as in Jha et al.[34]. First, I calculate the total number of blacks discharged from each hospital from FY1996 to 2002 in the entire data set. I count the length of time each site was in existence, to account for mergers and closures within the study period. For example, if a site only existed for 3 years and 3 months, I count the length as 3.25 years. After dividing the total number of black patients per site by the corresponding length of time, I obtain the average annual number of black patient for each site over the study period. Then, I rank VA sites from the lowest to the highest by the average annual number of black patient hospitalizations. As in Jha et al.[34], sites are classified into quartiles of the cumulative distribution of site-specific average annual volume of black patients.

All analyses will be limited to the sub-group of veterans younger than 65 years old and hospitalized with pneumonia. This subgroup was chosen for two reasons: 1) pneumonia had largest sample size across the six diagnostic conditions considered; and 2)the younger pneumonia patient data set had the maximum variance component of black race effect across all six diagnostic conditions and both age groups. For the pneumonia veterans younger than 65 years old, the first quartile (Q1) includes 108 sites with no more than 24 average annual black visits (Table I.1). There were 21 sites in Q2, 12 in Q3, and 9 in Q4. Kerft[36] has reported a 30/30 rule of thumb for experimental design in a multilevel model. The recommendation is that at least 30 sites and 30 individuals per site are needed to use multilevel models. Therefore, I choose the 42 sites in Q2-Q4 (Q24), where 75% of black patients are hospitalized, as a concentrated sample in this dissertation.

D.   HYPOTHESIS TESTING AND MODEL FITTING STRATEGIES

The same model fitting strategies will be used for the full sample and Q24 subsample. Before explaining the model fitting strategies, I will clarify the definition of random effect and the hypothesis test in the MLLM. Some authors[4][63] discuss the random slope as the race interaction with site. To keep the terminology simple, I split the random slope into two parts: the fixed effect and random effect of black race. The fixed effect of black race represents the average difference in log odds between black and white veterans within sites. The random effect of black race refers to the variation in the log odds associated with black race across sites.

Goldstein [25] discussed the approximate Wald test for both fixed and random effects (details in Section II.D.2) and has implement this method in MLwiN. I used this approximate Wald test to perform the hypothesis test in this software. In the MLwiN, we can fit a model and make hypothesis test in two ways 1) manually 2) by macro. Although both produce exactly the same result, in the 2-level logistic model, the parameter estimates from one way won't be recognized by the other way. To fit the model and do hypothesis tests manually, the MLwiN user Manual has step by step introduction[53]. To fit the model and perform the hypothesis test, I give a sample macro in the Appendix F.C and F.D. Before performing the hypothesis test, a contrast matrix needs to be defined in a free column for the corresponding hypothesis test, using **joint**, ie **joint c1 1 0 0 c1**. The hypothesis test on the fix effect and random effect is implement by function **ftest** and **rtest**. In the MLwiN, the parameter estimates are stored in the specific box and cell. For example, in a 2-level unadjusted RI model, ftest c1 will perform a hypothesis on the fixed effect of intercept term. Instead rtest c1, will perform a hypothesis test on the level 2 residual of site.

A standard Chi square with 1 degree freedom test is used to test the fixed effect of black race, using a cut point of 3.84 for a two side 0.05 level test. A mixture Chi-2 test with 1 and 2 degrees of freedom is used for the test for a variance component, using a one-sided 0.05 level test. Because the variance components are always larger than 0, a one sided 0.05 level test is applied to $H_o : \sigma^2_{\mu_i} >= 0$, a mixture Chi-2 distribution is suggested.[21] using a cut off value 5.14. Because of mixture Chi-2 distribution applied to random effect

hypothesis test estimates, only a range of P-value can be given. Estimation methods for variance components is very limited, and is an active research area, I will accept Goldstein's Wald test to test variance components and will not perform any simulation on the variance components.

The RIGLS PQL2 method will be used to implement the simulation study, because this method can fit a model in several second and is the most accurate method within quasi-likelihood estimation. However, the analytic variance formulae were derived using the MQL1 method. To compare the accuracy between the PQL2 and MQL1 methods in both study populations, I will fit the same RI model using IGLS MQL1 and perform the same hypothesis tests.

Model diagnostics are applied to test the normality of residual and identify outliers. A caterpillar plot [25] for the site level will be applied to explore the site outliers and check the normality simultaneously.

For the RI model, I will fit the model and do the hypothesis test using both the RIGLS PQL2 and IGLS MQL1. Three hypothesis tests will be performed: 1) fixed effect of site, 2) random effect of site, and 3) fixed effect of black race as well as model diagnostics.

For the RC model, I will fit the model and do the hypothesis test using both the RIGLS PQL2 and IGLS MQL1 methods. Four hypothesis tests will be performed: 1) fixed effect of site, 2) random effect of site, 3) fixed effect of black race, and 4) random effect of black race as well as model diagnostics.

The outline of model fitting strategies for either the full data or Q24 data are shown as below:

I. Fit the RI model using the RIGLS PQL2 method
    A. Hypothesis test on fixed effects: site and black
    B. Hypothesis test on random effect: site
    C. Model diagnostics
II. Fit the RI model using the IGLS MQL1 method
    A. Hypothesis test on fixed effects: site and black
    B. Hypothesis test on random effects: site
    C. Model diagnostics

III. Fit the RC model using the RIGLS PQL2 method

    A. Hypothesis test on fixed effects: site and black

    B. Hypothesis test on random effects: site and black

    C. Model diagnostics

IV. Fit the RC model using the IGLS MQL1 method

    A. Hypothesis test on fixed effects: site and black

    B. Hypothesis test on random effects: site and black

    C. Model diagnostics

Another concern for the RC logistic model is whether the random slope term is significantly different than zero. Conditional logistic regression is useful in investigating the relationship between an outcome and a set of prognostic factors in matched case-control studies, the outcome being whether the subject is a case or a control. The interaction (group*intervention) can be used to check whether the site and race interaction exists across the matched groups. From this conditional logistic model, we can assess whether the race effect varies across sites, without assuming normality. Stata clogit function is applied to fit this conditional logistic model with race and site interaction. Further more, the main effect conditional logistic model and 2-level RI model will be fitted by Stata using Gaussian Quadrature method. The estimate from Stata will be compared to PQL2 estimates from MLwiN to check the accuracy of PQL2.

E. SIMULATION METHODS

1. Simulation To Validate Analytic Results

In the section, I will apply Feiveson's [15] power simulation method to estimate post-hoc power in the simulation studies. Power is estimated by counting the proportion of rejection in the hypothesis test in the 2000 iterations. The hypothesis tests for both the random and fixed effects are Goldstein's asymptotic Wald tests[25]. The simulation studies are based on the observed site-specific racial distributions and parameter estimates obtained by fitting an unadjusted MLLM including only a fixed effect for black race.

The objectives of simulation are to 1) obtain the sample mean variance and compare it to the analytic results. 2) estimate the post-hoc power of black as a fixed coefficient in the RI and RC models in the full data set and the Q24 data; 3) based on the observed site-specific racial distributions in the pneumonia data, identify the effect size that can be detected with 80% power, with type one error 0.05 in a two-sided test.

2. Fit Unadjusted Model to the Volpp Data in Table IV.2 and Table IV.4

I need to fit the RI or RC model to one of the study populations to get the true parameter estimates for these model. The outline to fit the unadjusted model is shown below. In the Appendix F.C, the MLwiN macro syntax is attached for the following steps with detail comments

I. Fit the RI (or RC) model using RIGLS PQL2

   A. Read in the Pneumonia data

   B. Set up the RI or RC model

   C. Run the model

   D. Copy empirical parameter estimate from c1096-c1099 to column c106-c109 (C1096 to C1099 store the parameter estimates in each model fitting. To avoid overlay of the unadjusted parameter estimates of Volpp data, I reserve them in other location)

   E. Erase column c1096-c1099, to clear the variance covariance structure to be ready for simulation

F. Save this worksheet containing the parameter estimates for the Volpp study

This provide the "True" parameter values for the subsequent simulation. To make the program efficient, I also defined the hypotheses contrast columns in this file. In the simulation studies, the hypothesis test can be performed immediately.

3. Simulated on Outcome Data

From the parameter estimates$(X\hat{\beta}, Z\hat{\mu})$ in Appendix III.E.2, I used the simulation function (Simu) in MLwiN to simulate the random effect $(Z\mu)$ and prediction fixed effect function (predict) to simulate the fixed effect$(X\beta)$. Then, I apply an anti-logistic transformation $(1 + exp^{(-x)})$ to the simulated linearized probability $(\hat{\pi}^* = X\hat{\beta} + Z\hat{\mu})$. The simulated binary outcome will follow the binomial distribution of bin(M, $\hat{\pi}$). Lastly, I fit the model with a dummy variable for black race using the new simulated outcome and conduct the hypothesis tests. After completing 2000 iterations, I calculate the post-hoc power and sample mean variance using SAS macro program. The simulation outline is show below and the detailed MLwiN and SAS macro codes are shown in Appendix F.D and Appendix F.E, respectively.

I. Do below loops T=2000 times

    A. Assign inital parameter estimates in column c1096- c1099 from c106-c109

    B. Simulate estimates of fixed effect

    C. Simulate estimates of random effect

    D. Computer the linear predictor from the parameter estimates

    E. Calculate the probability of response by using anti-log$(X\beta + Z\mu)$ transformation

    F. Simulate the new binary response variable follow bin(n, π)

    G. Fit the RI or RC model using this simulated response variable

    H. Conduct the hypothesis test for the fixed and/or random effect of black race

    I. Store the parameter estimates and hypothesis test result needed for variance and power calculations.

II. Calculate the simulated power $= \frac{\text{total number reject } H_o}{T}$

III. Calculate the mean simulated variance of the fixed effect of black race $= \frac{\sum var(black)}{T}$

IV. Calculate variance ratio$= \frac{\text{mean simulated variance}}{\text{empircal variance}}$

Using the simulated variance ratio, a comparison between simulated variance and empirical variance to assess how accurate my simulation algorithms are. The simulated variance is collect all the variance from each replication to obtain the simulated mean variance. Another option is using simulated estimate variance, the variance of the parameter estimate. In my dissertation, I use the simulated mean variance (as did Moerbeek). At the same, the accuracy on the variance estimate is an important criteria in experimental design.

4. Detect Race Parameter Estimate as Fixed Effect to Obtain Power 0.8

The objective of this subsection is to find an appropriate range of fixed coefficients for race in the 2-level logistic model that can be detected with approximating 80% power using the racial distribution in a defined study population. In the above simulation algorithm, I will replace the race parameter in Appendix 3.1.A. A from +/-0.1 to +/-0.9 using a grid 0.1. For each designated parameter estimate, I will estimate the power. I will end the simulation when the power approaches 80%. If the power reaches 80% between $\beta_{1,H_{o1}}$ and $\beta_{1,H_{o2}}$, I will do further simulation between these values using grid 0.01. A plot of power vs. the log odds ration can be drawn.

The modification to the above are shown below

1.A' Replace the parameter estimate of black to the designated value β_{1,H_o}, using grid 0.1

V. Restrict the range of $[\beta_{1,H_{o1}}, \beta_{1,H_{o2}}]$ to values that bracket 80% power.

VI Do above step in the restricted range using grid 0.01

IV. RESULTS

A. DESCRIPTIVE ANALYSIS OF PNEUMONIA PATIENTS YOUNGER THAN 65 IN THE VOLPP STUDY

The Volpp study includes 37,111 hospitalizations for pneumonia patients younger than 65 years old from FY1996 to 2002 in 149 VA sites, nationally. This number excludes females, Hispanics or other races, as well as non-veteran patients treated at those facilities or who lived outside the 50 states, admissions to non-acute facilities, re-admissions within 30 days with the same condition, and admissions after a hospital transfer. In the multilevel structure, the cluster is the site and the individual level is the hospitalization. My study compares the mortality within 30 day admissions for black patients with that of white patients. Black race, coded as 1 for black and 0 for white, is the independent variable of primary interest. Black race is considered as a fixed effect in the RI model and both fixed and random effects in the RC model.

The racial distributions are dramatically unbalanced across sites, as shown in Table IV.1. More than half (51.61%) of the patients overall were hospitalized in the 109 sites in the lowest quartile of average annual black patient volume, i.e the sites where only 25% of black patients were hospitalized. In the highest quartile, 25% of blacks were hospitalized at only 9 sites. The geographic location for these sites are shown in Figure IV.1. The relative proportion of black patients within sites increases by quartile with black comprising 13.08% of hospitalizations in Q1 and 57.25% of hospitalizations in Q4. The quartile specific white mortality is higher than the corresponding black mortality. Except for blacks in the highest quartile, race specific and overall mortality increase with quartile.

By scanning the site and race specific mortality in all black and white pneumonia patients

Table IV.1: Distribution of VA Sites by Quartiles of Black Volume for Black and White Veterans Younger than 65 Years Old Hospitalized with Pneumonia, and corresponding 30-day Mortality

Black Quartile *	Site (N)	Hospitalizations (M)	Black (%)	30-Day Mortality		
				Black	White	Overall
Q1	107	19,154	13.08	6.43	7.27	7.16
Q2	21	7,913	34.68	6.63	8.01	7.53
Q3	12	4,701	53.37	7.69	8.85	8.23
Q4	9	5,343	57.25	7.00	9.15	7.92
Total	149	37,111	29.15	6.93	7.71	7.49

* Ranked by site specific average annual black volume

younger than 65 years old, black mortality is zero at 49 sites (4989 hospitalizations), including four sites (sites 18, 67, 77, and 88; total 44 hospitalizations in these four sites) with no black or white mortality. Site 143 has no white deaths and one black death (13 hospitalizations) and eight sites (2, 33, 60, 67, 72, 91, 137, and 145) with no black hospitalizations. All these sites belong to the first quartile of average annual black patient volume. The remaining 44 sites have white mortality but no black mortality. These sites with no black and white deaths ("Uniform cases" [4]) can lead to unreliable parameter estimates for the RI model or conditional logistic model.

Figure IV.2 shows scatter plots of the site-specific total number of black patients vs. the proportion of black patients at (a) overall 149 sites , (b) for the 42 sites in Q2-Q4, and (c) by quartiles of black patient volume. These scatter plots show that sites with a greater number of blacks tend to have a higher proportion of black patients, particularly in quartile Q24. Some sites have a large proportion of black patients but few black patients, which may be explained by site mergers or closures. Using pairwise correlation coefficient tests, all the correlation coefficient are large than 0.99 (P < 0.001). Therefore, the site specific black proportions are highly correlated to the corresponding numbers of black patients.
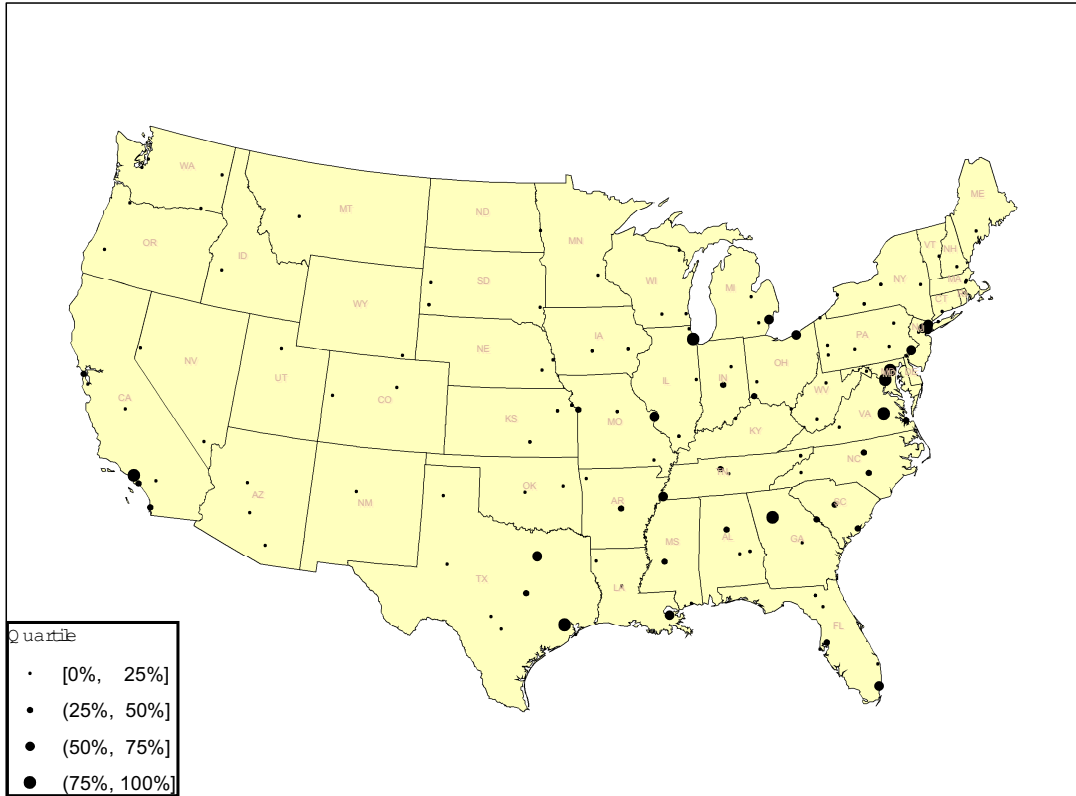
Figure IV.1: Geographic Location for VA Sites by Quartiles of Average Annual Black Patient Volume

Figure shows average annual number of black patients vs. the proportion black in the same format as in Figure IV.2. These plots shows the similar pattern to Figure IV.2. The few discrepancies between total number of average annual volume are due to sites that were not in existence in the entire study period. Using pairwise correlation coefficient tests, all the correlation coefficient are large than 0.99 (P ¡0.001). Therefore, the site specific black proportions are highly correlated to average annual black patient number in all above three conditions.

The cumulative distributions of the site and race-specific patient numbers are shown in Figure 4(a) for over all 149 sites and Figure IV.4(a) for the 42 sites in Q2-Q4. Figure IV.IV.4 illustrates that 80% of black patients had been hospitalized in sites with no more than 117 black patients. Only six sites have more than 300 hospitalizations of black patients for pneumonia annually (on average), three sites have more than 400, and one site has more than 500. In contrast, 80% of white patients had been hospitalized at sites with fewer than 283 annually (on average) hospitalizations; twenty-one sites had more than 300 white hospitalizations, eight sites had more than 400, and three had more than 500. Figure IV.4(b) shows the corresponding cumulative distributions for 42 sites in Q2-Q4. The cumulative distributions are much less disparate when the sites with relatively few blacks are excluded.

The above results demonstrate the dramatic racial imbalance at these sites. To examine how imbalance will affect the experimental design. I will do the analysis on both the entire population and patients hospitalized at the most concentrated sites (Q2 to Q4). I will compare the observed unbalanced design with the relativing more balanced design.
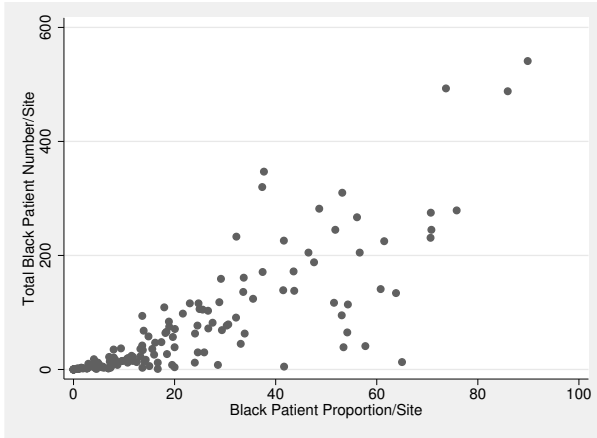
(a) Overall
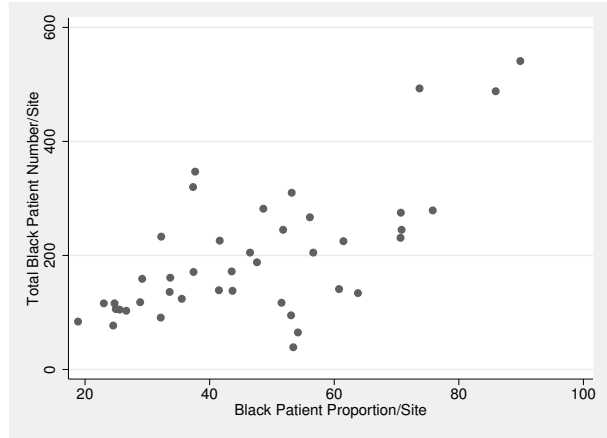
(b) Q24
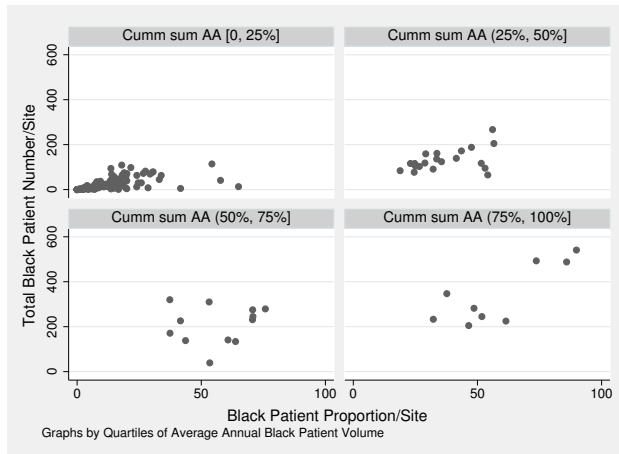
(c) By Quartiles

Figure IV.2: Scatter Plot of Site-Specific Total Black Patient Number vs. Proportion Black (a) Over All 149 Sites, (b) For the 42 Sites in Q24, and (c) by Quartile of Black Patient Volume
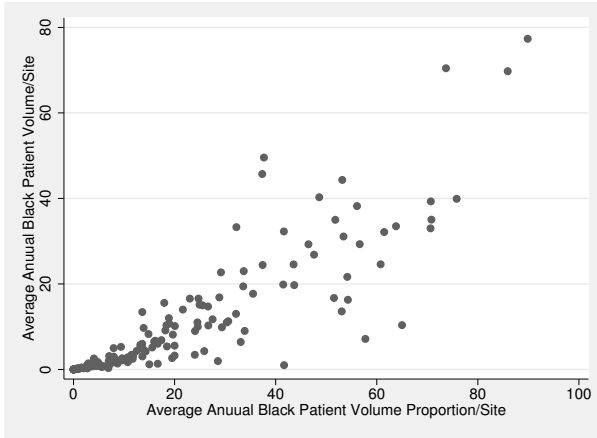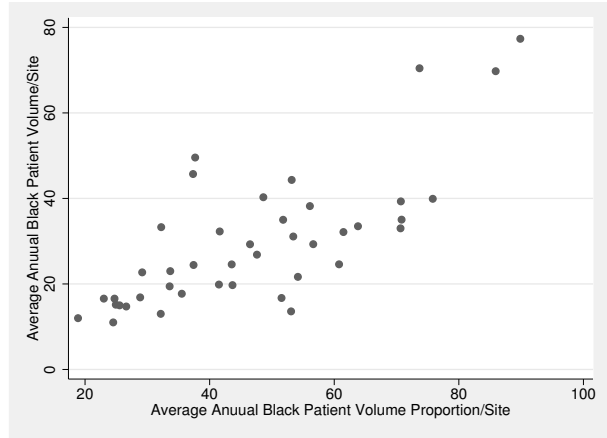
(a) Overall

(b) Q24
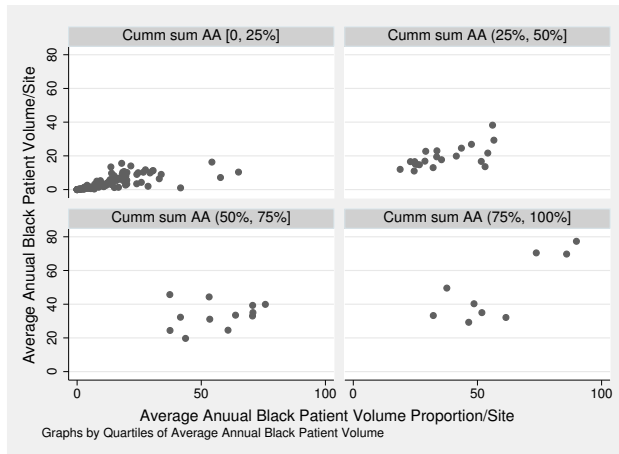
(c) By Quartiles

Figure IV.3: Scatter Plot of Site-Specific Average Annual Black Patient Number vs. Proportion Black (a) Over All 149 Sites, (b) For the 42 Sites in Q24, and (c) by Quartile of Black Patient Volume
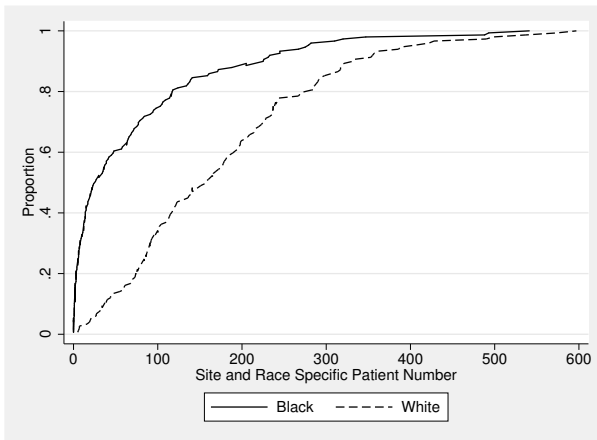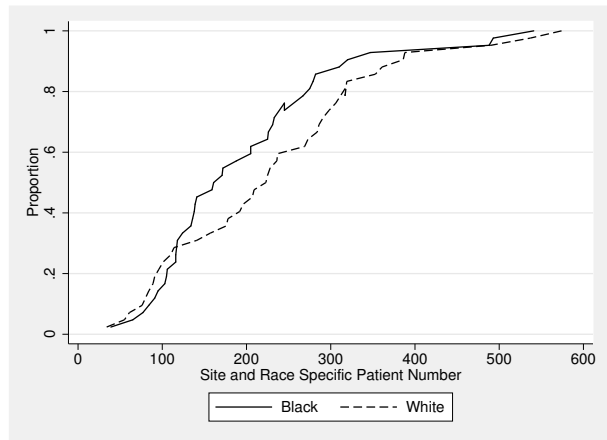
(a) Over All   (b) Quartiles 2-4

Figure IV.4: Race Specific Cumulative Distributions vs. Race and Site-Specific Total Numbers of Patients Aged Less Than 65 Years Old with Pneumonia (a) Over All 149 Sites and (b) for Quartile 2-4

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B.   PARAMETER ESTIMATION

1.   Model Fitting, Entire Population

Without any adjustment, the estimated race specific 30 day mortality is 6.9% for blacks and 7.7% for whites, with a 0.89 odds ratio for black relative to white veterans. I fit the RI and RC models using the RIGLS PQL2, which is optimal within the quasi-likelihood approximation methods.

Table IV.2 and Table IV.3 summarize the estimate log odds of 30-day mortality for black relative to white veterans in a two-level logistic model using PQL2 and MQl1, respectively. Appendix E includes the images of the corresponding MLwiN results.

Table IV.2: Estimated Log Odds of 30-day Mortality for Black Veterans Relative to White Veterans in 2-Level Logistic Models Fit Using PQL2, for Pneumonia Patients Younger Than 65

Model	Parameter	Fixed Effect			Random Effect		
		Est.	SE	Chi-2	Est.	SE	Chi-2
RI	cons	-2.52	0.03		0.05	0.01	13.67
	black	-0.11	0.05	5.67			
RC	cons	-2.51	0.03		0.04	0.01	7.28
	black	-0.16	0.06	6.65	0.09	0.05	4.08

Note: The cut point for the fixed effect is 3.84 as $chi^2_{1,0.05}$ and for random effect is 5.14 by using a mixture of Chi-Square distributions of $chi^2_{1,0.05}$ and $chi^2_{2,0.05}$

In Table IV.2, the Chi^2 statistic for the random effect of the hospitals is 7.28, which is larger than the cut off value of the mixture $Chi^2_{1,0.05}$ and $Chi^2_{2,0.05}$, 5.14. Therefore, both the RI and RC logistic models indicate significant site to site variation in mortality ($P < 0.001$) for the random intercept term. For the fixed effect of black race, the ORs of blacks are 0.89 ($e^{-0.11}$) and 0.86 ($e^{-0.16}$) relative to whites for the RI and RC models, respectively. The corresponding Chi^2 statistics are 5.67 and 6.65. Both Chi^2 statistics are larger than the cut off value $chi^2_{1,0.05}$, 3.84. Black veterans have lower mortality than white veterans hospitalized in the same site(P=0.017). The random effect of black race does not show significant variation in the OR of blacks across sites (Chi^2=4.08<5.14).

Corresponding MQL1 results are shown in Table IV.3. The MQL1 method assumed that

Table IV.3: Estimated Log Odds of 30-day Mortality for Black Veterans Relative to White Veterans in 2-Level Logistic Models Fit Using MQL1, for Pneumonia Patients Younger Than 65

Model	Parameter	Fixed Effect			Random Effect		
		Est.	SE	Chi-2	Est.	SE	Chi-2
RI	cons	-2.48	0.02		0.00	0.00	#
	black	-0.12	0.04	6.72			
RC	cons	-2.49	0.03		0.04	0.014	7.45
	black	-0.12	0.06	3.50	0.11	0.05	5.01

no estimate exists for this term
Note: The cut point for the fixed effect is 3.84 as $chi^2_{1,0.05}$ and for random effect is 5.14 by using a mixture of Chi-Square distributions of $chi^2_{1,0.05}$ and $chi^2_{2,0.05}$

the variance components are 0 in the previous iteration step. The parameter estimates in the Volpp study indicate that the MQL1 may not be a good estimation method for these data. The MQL1 parameter estimates for other terms are similar to the PQL2 results, yielding the same conclusions as for PQL2. There exist variation in mortality both within and across sites. Black patients have significantly lower mortality than white patients within sites. There is no significant variation in the OR for black race across sites.

2.   Model Fitting, Site Q2-Q4

The Q2-Q4 sub-sample focuses on the sites where the majority of black patients are hospitalized. Results for the subsample, which includes in 42 sites with 17,957 hospitalizations, are shown in Table IV.4 and Table IV.5 for the RI and RC logistic models using PQL2 and MQL2, respectively.

From PQL2 estimation, the race specific mortality varies significantly across sites in the RI model (Chi^2=5.11> 3.84). Similarly, the race specific mortality varies significantly across sites in the RI model fit using MQL2 (Chi^2=4.94> 3.84). Blacks show significantly lower mortality than whites within the same site (log odds=-0.13 with OR=0.88 for both PQL2 and MQL1 estimates).

In the RC model, the race specific mortality varies significantly across sites for both the

PQL2(Chi^2=9.01> 5.14) and MQL1(Chi^2=9.21> 5.14) methods. The log OR for black race is more extreme using PQL2 (log OR=-0.19, OR=0.83) than the log OR= -0.14 (OR=0.87) using MQL1. The log OR for the fixed effect black race is non-significant in the MQL1 method (OR=-0.14, Chi^2=2.87 < 5.14), but is significant(OR=-0.19, Chi^2=5.59 > 5.14) using PQL2. Corresponding standard error estimate using PQL2 (Table IV.4) and MQL1 (Table IV.5) are equal to at least two decimal places.

Table IV.4: Estimated Log Odds of 30-day Mortality for Black Veterans Relative to White Veterans in 2-Level Logistic Models Fit Using PQL2, for Pneumonia Patients Younger Than 65 in Q2−Q4

Model	Parameter	Fixed Effect			Random Effect		
		Est.	SE	Chi-2	Est.	SE	Chi-2
RI	cons	-2.44	0.06		0.07	0.02	9.01
	black	-0.13	0.06	5.11			
RC	cons	-2.42	0.05		0.04	0.02	3.17
	black	-0.19	0.08	5.59	0.12	0.06	4.00

Note: The cut point for the fixed effect is 3.84 as $chi^2_{1,0.05}$ and for random effect is 5.14 by using a mixture of Chi-Square distributions ($chi^2_{1,0.05}$ and $chi^2_{2,0.05}$)

Table IV.5: Estimated Log Odds of 30-day Mortality for Black Veterans Relative to White Veterans in 2-Level Logistic Models Fit Using MQL1, for Pneumonia Patients Younger Than 65, sites in Q2−Q4

Model	Parameter	Fixed Effect			Random Effect		
		Est.	SE	Chi-2	Est.	SE	Chi-2
RI	cons	-2.41	0.06		0.07	0.02	9.21
	black	-0.13	0.06	4.94			
RC	cons	-2.40	0.05		0.04	0.02	3.09
	black	-0.14	0.08	2.87	0.12	0.06	4.36

Note: The cut point for the fixed effect is 3.84 as $chi^2_{1,0.05}$ and for random effect is 5.14 by using a mixture of Chi-Square distributions ($chi^2_{1,0.05}$ and $chi^2_{2,0.05}$)

3. Test Race and Site Interaction in Conditional Logistic Regression

For the conditional logistic model using the full pneumonia data, the uniformity[4] that exists for 49 sites with no variation in race-specific outcome leads to infinite parameter estimates.

The estimates from the conditional logistic model with site by race interaction term are unreliable with many infinite parameters. The output consumes more than 100 pages, I selected partial results (in Appendix F.G). The Chi^2 test for the interaction term between sites and race is 110.49 (P=0.95 df=136). There is no significant interaction between race and site. In the Q2-Q4 data the uniform sites have been excluded, which leads to reasonable parameter estimates with a reliable Chi^2 test of the interaction terms. The Chi^2 test for the interaction term between sites and race is 60.71 (P=0.02, df=41) indicating a significant interaction in this subset of sites.

4. Model Diagnostics for MLwiN Models

A caterpillar plot[25] displays the residuals in ascending order with their 95% confidence limits. The site specific 95% CI plot will not overlay the central line (y=0), when there are poorly fitted sites. In the RI model for the full data set(Figure IV.5), the outliers from the left side to the right sites are 105(purple), 148 (yellow) , 127 (green), 24(blue), 73 (red). These data are described in Table I.2. When the RC model is fit to the same data with the same highlighted colors for the outliers as in RI model, the poorly fitted sites from the left side to the right sites are 127 (green), 24(blue), 73 (red) (Figure IV.6). For the Q2-Q4 subsample in the RI model, there are no poorly fitted sites. In the RC model for the Q2-Q5 subsample, two poorly fitted sites (42 and 23) exist. All the above plots have a linear trend, which supports the normality of these residuals.

The main effect conditional logistic model and the RI parameter estimates of race, using both Stata and MLwiN PQL2, are shown in Table IV.6. The parameter estimates in the RI model using Stata via numerical integration are virtually identical to those obtained in MLwiN using PQL2. The parameter estimates from the conditional logistic model and RI model are similar for the full data but somewhat less so in Q2-Q4.
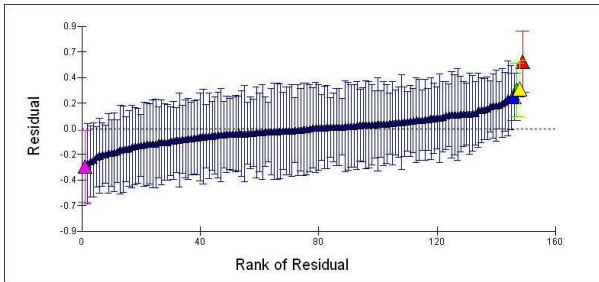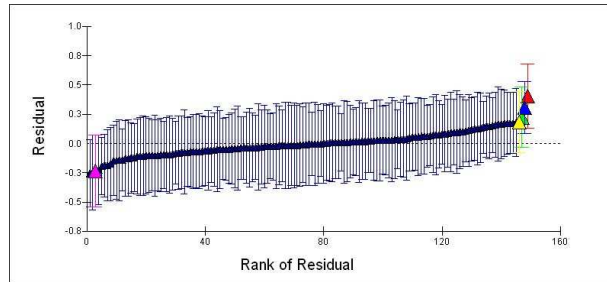
(a) RI   (b) RC

Figure IV.5: Caterpillar Plot for the Full Data
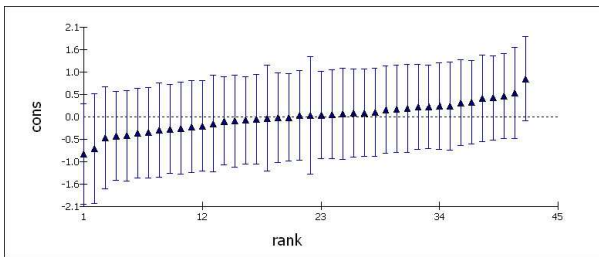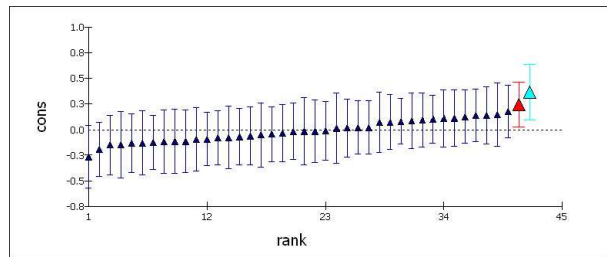
(a) RI   (b) RC

Figure IV.6: Caterpillar Plot for the Q2-Q4 Data

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Table IV.6: Estimated Log Odds of 30-day Mortality for Black Veterans Relative to White Veterans in Logistic Models for Pneumonia Patients Younger Than 65 Years

Model	Data	$\hat{\beta}_1$	SE	P Value	log likelihood
Conditional logistic model (Stata)	full	-0.12	0.05	0.02	-9418.40
	Q24	-0.10	0.06	0.09	-4755.76
RI (Stata)	full	-0.11	0.05	0.02	-9846.72
	Q24	-0.14	0.06	0.02	-4906.90
RI (MLwiN)	full	-0.11	0.05	0.02	#
	Q24	-0.13	0.06	0.01	#

\#   the log likelihood estimates are crude in PQL2 and not available in MLwiN

C. ANALYTIC VARIANCE OF THE FIXED EFFECT OF BLACK RACE

In this section, I evaluate the derived variance formulae (in Table III.6, III.7, III.9, III.8) under different design scenarios based on the observed site specific race distribution as in the Volpp data and the parameter estimates obtained using PQL2 (Table IV.2 and Table IV.4) for over all data and subsample, respectively. For scenarios with balanced sample size across sites in the entire population, the average sample size is $\bar{n} = 37111/149 = 249.07$ for each site. The average number of black patients per site is 72.60 and the average black proportion is 22.22%. The sub-sample of 42 sites includes 17,957 patients with an average of 197.91 blacks (46.96%) per site.

I calculated hypothetical site-specific sample sizes for all scenarios except the total unbalanced observed scenario (U_{w_j}), based on features of the Volpp data. This was done separately for the entire sample and subsample. For scenarios $B_{\bar{w}}$ and $U_{\bar{w}}$, which are balanced and unbalanced scenarios with a common proportion of black veterans, I multiplied the assumed average proportion black by the average sample size per site for $B_{\bar{w}}$, and by the observed site-specific sample size for $U_{\bar{w}}$. Scenario B_{w_j} has an assumed common sample size across sites and site specific sample weights; scenario u_{w_j} has the observed site-specific distribution. For the scenarios with variable proportion black (B_{w_j} and U_{w_j}), I multiplied the site specific proportions black by the approximate race specific denominator. These quantities are summarized in Table IV.7.

Imbalance in the design increased variance of the fixed effect for both the RI and RC model as shown in Table IV.8. It shows the analytic variance on assumed balanced scenarios are 0.0016 and 0.0022 for RI and RC models, respectively, using full data and 0.0032 and 0.0060 for RI and RC model using subsample of 42 sites. Compared to the variance estimate obtained by fitting th PQL2 model to these hypothetical data, the corresponding analytic variances are 0.0022 and 0.0036 for RI and RC using all data, and 0.0035 and 0.0066 for RI and RC in the subsample of 42 sites.

Using the derived analytic formula for fixed effect of black race (Table III.6, III.7, III.9, III.8), I find the variance formulae for the fixed effect are the same for scenario $B_{\frac{1}{2}}$ as $U_{\frac{1}{2}}$, and $B_{\bar{w}}$ as $U_{\bar{w}}$. I then apply a site sample weight (black proportion) varying from 0.1 to

0.9 with 0.1 grid. Table IV.9 shows the variance of the fixed effect black race in the entire study for designs with the same proportions blacks, Table IV.10 shows comparable results in the sub-sample of sites that hospitalized the majorities of black veterans. Moerbeek compares the accuracy of her analytic variance formula by the ratio factor, defined as the ratio of simulation sample mean variance divided by analytic variance. Instead, I compare analytic ratio of the analytic variance to the true empirical variance. Using analytic ratio, the simulation study is not required. In both Table IV.9 and Table IV.10, the minimum variance is observed at 0.5, and increased in both directions away from 0.5. Relative to the variance estimate obtained by fitting the PQL2 method to these hypothetical data, the corresponding analytic variance is an underestimate for proportions black in the range of 0.3 to 0.7 in the RI model with ratios < 1, and is an overestimate for the more extreme proportions for the full data set (Table IV.9). In the RC model, the analytic variance is an overestimate only for the most extreme probabilities considered (0.1 and 0.9). For the subsample, the analytic variance is an overestimate except balanced case (0.47, or 0.5). In contrast, the analytic variance is an underestimate in the range of 0.4 to 0.7. For the more extreme proportions, the more overestimate.

Scenario B_{w_j} has an assumed common sample size across sites and site specific sample weights (Table IV.11) and scenario U_{w_j} has the observed site-specific distributions (Table IV.12). The variance ratio furthest from unity in the RC models with site specific weights for the entire data. As in the other scenarios considered, variances are smaller in the RI model than the corresponding quantities in the RC model.

The variance estimates in Table IV.9 and Table IV.10 are summarized graphically in Figure 7(a) for the full data and Figure 7(b) in the 42-site subsample. Extreme imbalance has much more effect on the variance estimate in the subsample, which includes 28.2% of sites.

Table IV.13 and Table IV.14 compare the analytic results (unbalanced everywhere and unbalanced sample size with site specific proportions) to the MQL1 and PQL2 estimates for the full data and subsample. Using the analytic variance with the same site-specific weight or the imbalance ratio of the analytic variance and empirical variance using the true race distribution can be used to quantify the effect of imbalance. In the full data, the RI model

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has a lower imbalance ratio than the RC model (1.10 vs. 1.33)for PQL2 (Table IV.13). In contrast, the imbalance ratio are higher in the RC model for the Q2-Q4 subsample($>$1.6 vs 1.1) for PQL2 (Table IV.14). Using the true race distribution, the imbalance ratios are 1 for the full data in both RI and RC models. In the subsample, the imbalance ratios are 1.6 and 1.0 for RI and RC models, respectively. In the full data, we have a lot sites with extreme race proportion. In the subsample, we have exclude the uniform sites to fit the multilevel model better.

Table IV.7: Summary Information from the Volpp Data for the Var(Black) Calculation

Demographic Data	Entire Sample		Subsample	
Number of patients (M)	37,111		17,957	
Number of sites (N)	149		42	
Average sample size per site (n)	249.07		427.55	
Average black number ($\bar{n}_{jB} = \sum n_{jB}/N$)	72.597		197.91	
Average % Black ($\bar{W} = \sum p_{black}/N$)	22.22		46.96	
Parameter Estimates from PQL2				
	RI	RC	RI	RC
$\hat{\beta}_0$	-2.517	-2.509	-2.439	
$\hat{\beta}_1$	-0.113	-0.155	-0.134	-0.191
$\sigma^2_{\mu_0}$	0.048	0.036	0.069	0.036
$\sigma^2_{\mu_1}$		0.094		0.116
$\frac{\sigma^2_{\mu_1}}{N}$		0.0063		0.0028
$var(\varepsilon^*_{..B})$	15.95	16.42	15.18	15.6186
$var(\varepsilon^*_{..W})$	14.47	14.37	13.55	13.2791

Table IV.8: Empirical Variance and Assumed Balanced Analytic Variance

Var(Black)	Entire Sample		Subsample	
	RI	RC	RI	RC
Analytic (balanced)	0.0016	0.0022	0.0032	0.0060
Empirical	0.0022	0.0036	0.0035	0.0066

Table IV.9: Analytic Variance of the Fixed Effect of Black Race Assuming a Common Percent Black Across Site ($B_{\frac{1}{2}}$, $B_{\bar{w}}$, $U_{\frac{1}{2}}$, and $U_{\bar{w}}$) in the Full Sample

Weight	Var in RI	Ratio	Var in RC	Ratio
0.1	0.00473	2.14	0.00549	1.52
0.2	0.00264	1.19	0.00333	0.92
0.22 #	0.00244	1.10	0.00312	0.86
0.3	0.00199	0.90	0.00266	0.73
0.4	0.00172	0.78	0.00238	0.66
0.5*	0.00164	0.74	0.00229	0.63
0.6	0.00169	0.76	0.00234	0.64
0.7	0.00191	0.86	0.00255	0.70
0.8	0.00249	1.12	0.00312	0.86
0.9	0.00438	1.18	0.00500	1.38

ratio=$\frac{analytic\ variance}{empirical\ variance}$

#: for B_{w_j} and U_{w_j} for scenario with common sample size

across site or observed Site Specific Weights

*: Empirical variance is 0.0022 and 0.0036 for RI and RC model

*: scenario $B_{\frac{1}{2}}$ or $U_{\frac{1}{2}}$

Table IV.10: Analytic Variance of the Fixed Effect of Black Race Assuming a Common Percent Black Across Site ($B_{\frac{1}{2}}$, $B_{\bar{w}}$, $U_{\frac{1}{2}}$, and $U_{\bar{w}}$) in the Sub-Sample

Weight	Var in RI	Ratio	Var in RC	Ratio
0.1	0.0093	2.85	0.0123	1.87
0.2	0.0052	1.59	0.0080	1.22
0.3	0.0039	1.20	0.0067	1.02
0.4	0.0034	1.03	0.0062	0.94
0.47 #	0.0032	0.99	0.0060	0.92
0.5*	0.0032	0.98	0.0060	0.91
0.6	0.0033	1.01	0.0061	0.93
0.7	0.0037	1.14	0.0065	0.99
0.8	0.0048	1.48	0.0075	1.14
0.9	0.0085	2.61	0.0111	1.69

ratio=$\frac{analytic\ variance}{empirical\ variance}$

#: for B_{w_j} and U_{w_j} for scenario with common sample size across site or observed Site Specific Weights

*: Empirical variance is 0.0033 and 0.0066 for RI and RC model

*: scenario $B_{\frac{1}{2}}$ or $U_{\frac{1}{2}}$

Table IV.11: Variance with a Common Sample Size Across Sites and Observed Site-Specific Weight(W_{w_j})

Data	RI	Ratio(%)	RC	Ratio
Full	0.0024	1.10	0.0031	0.86
Q2-Q4	0.0032	0.99	0.0060	0.91

ratio=$\frac{analytic\ variance}{empirical\ variance}$

Table IV.12: Variance with an Observed Site-Specific Sample Sizes and Weights(U_{w_j})

Data	RI	Ratio	RC	Ratio
Full	0.0022	0.91	0.00266	0.73
Q2-Q4	0.0032	0.99	0.0060	0.91

ratio=$\frac{analytic\ variance}{empirical\ variance}$
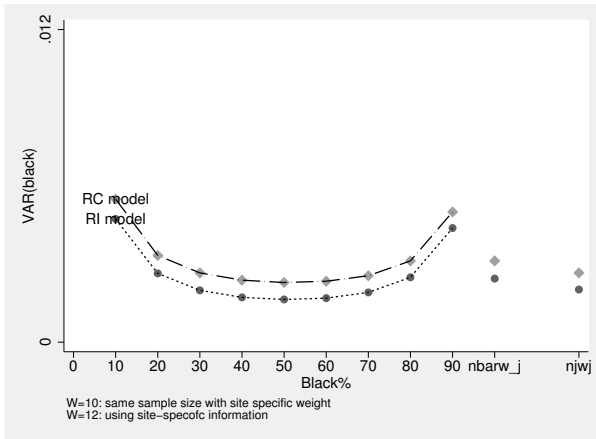
(a) Full data
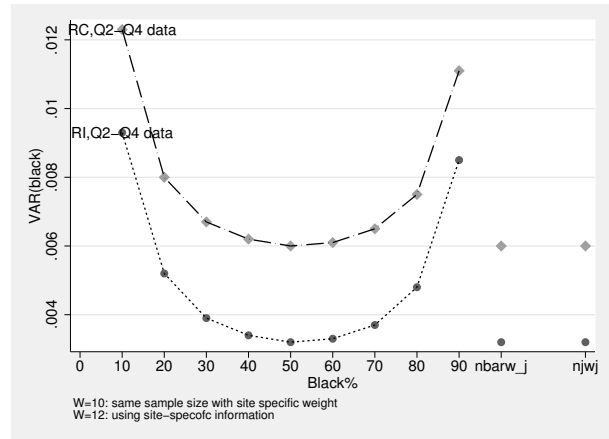
(b) Q2-Q4 Subsample

Figure IV.7: Analytic Variance of Fixed Effect of Black Race for the RI and RC Models Under Different Scenarios for the a) Full Data and (b) 42-Site Subsample

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Table IV.13: Variance of Fixed Effect Black Race in Analytic (U_{w_j} and $U_{\bar{w}}$ and Quasi-Likelihood Estimates, Full Data

Method	var(black)		Ratio to $\bar{w}$	
	RI	RC	RI	RC
PQL2	0.0022	0.0036	1.10	1.33
MQL1	0.0023	0.0036	1.15	1.33
Analytic($\bar{w}_j$)**	0.0020	0.0027	1.00	1.00
Analytic($\bar{w}$)*	0.0020	0.0027	1.00	1.00

* use site specific weight

** use true race distribution

Table IV.14: Variance of Fixed Effect Black Race in Analytic (U_{w_j} and $U_{\bar{w}}$) and Quasi-Likelihood Estimates, Q2-Q4 Subset

Method	var(black)		Ratio to $\bar{w}$	
	RI	RC	RI	RC
PQL2	0.0035	0.0066	1.75	1.10
MQL1	0.0035	0.0066	1.75	1.10
Analytic**	0.0032	0.0060	1.60	1.00
Analytic($\bar{w}$)*	0.0020	0.0060	1.00	1.00

* use site specific weight

** use true race distribution

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D. SIMULATION RESULTS

The results of the simulation study using the simulation methods in Chapter III.E will be reported in this section. These results are based on the site-specific racial distribution in Table I.2 for both the entire sample and the subsample of Q2-Q4. Both the 2-level RI and RC logistic models were considered.

1. Comparison of Mean Simulated Variance to Empirical Variance

To evaluate the simulation algorithm, I compare the mean simulated variance in the RI and RC logistic models for the full data set and 42 sites sub-sample to the corresponding empirical estimates (Table IV.15). The simulated variance of the fixed effect black race is close to the empirical variance in the RI logistic model for both populations, and in the RC for the entire data set. For the RC logistic model using the 42 site subsample, the PQL2 estimates were reported in Table IV.4. During the simulation, an unknown convergence problem occurred every 1-2 loops, which maybe due to the relatively small number of sites. Another possible reason is the PQL2's limitation. Convergence concerns have been reported [45]. Except in this convergence problem, my simulation algorithm appears to be accurate.

Table IV.15: Mean Simulated Variance and Empirical Variance of Fixed Effect of Black Race Estimates in Full Data and 42-Site Subsample

Data Set	Var(Black)					
	RI			RC		
	Simulated	Analytic	Empirical	Simulated	Analytic	Empirical
Full data	0.0023	0.0020	0.0022	0.0036	0.0027	0.0036
Q24	0.0035	0.0032	0.0035	$N.E^*$	0.0060	0.0066

N.E.   not estimable

Figure IV.8 and Figure IV.9 show histogram plots of simulated variances with a kernel density estimate for the full data using the RI and RC models, respectively. Figure IV.9

shows a histogram plot of simulation variance with a kernel density estimate for the Q2-Q4 subsample using the RI models. As mentioned above, the RC model has convergence problems and is not estimable. The kernel density estimate using the Epanechnikov Kernal is implemented in Stata 9.2 SE. In the full data set, the histogram plots shows that the simulated variances of the fixed effect of black race are centered around the empirical estimates and are approximate normal(Figure IV.8). The RC model has a large variance compared to the RI model (Figure IV.9). In the Q24 data, the simulated variances appear to have a bimodal distribution (Figure IV.D.1). Comparing the analytic results to simulated mean and empirical variance, the analytic results are downwardly biased. The center vertical line in the above three histograms are the empirical variances in the corresponding scenarios.
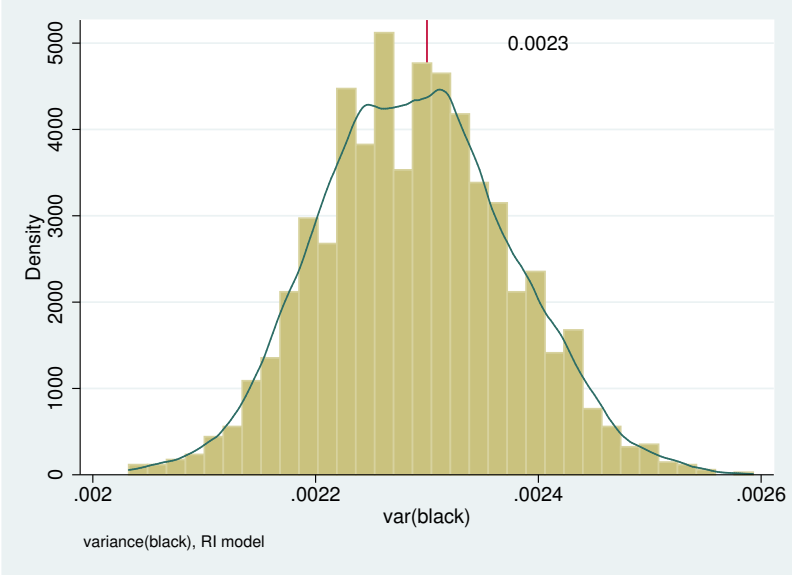
Figure IV.8: Simulated Variances of Fixed Effect of Black Race for Full Data Using the RI Logistic Model (2000 iterations)

2. Power Issues

The post-hoc power to detect the empirical log odds of 0.0022 and 0.0036 for the RI model is 65.5% for both the full data set and Q24, and 74.4% for the RC model with log odds of 0.0036 in the Q2-Q4 subsample.
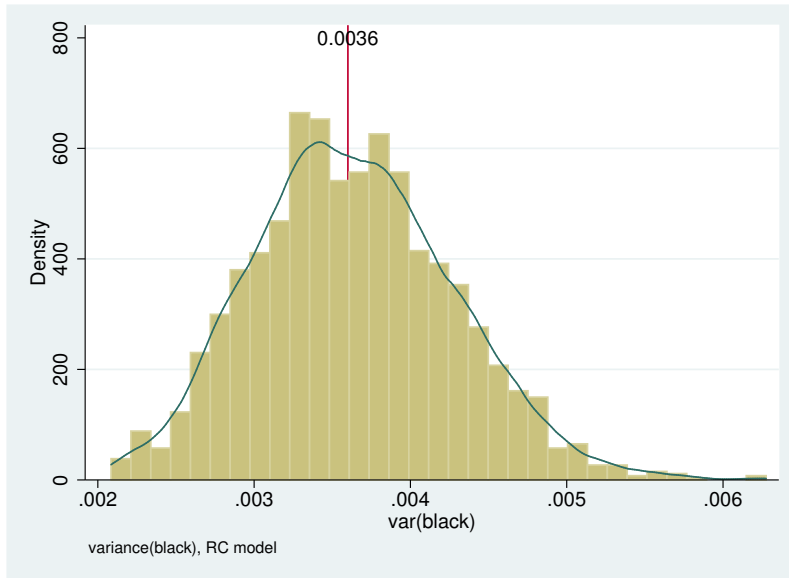
Figure IV.9: Simulated Variances of Fixed Effect of Black Race for Full Data Using the RC
Logistic Model (2000 iterations)

The following is the variance of race in three scenarios: 1) the RI model in full data; 2)
the RC model in full data; and 3) the RI model in the Q24, restricting the range of +/-0.1
to +/-0.2. To identify the black log ORs of mortality that can be detected with 80% power,
I run the simulation between this range with grid 0.01.

Figure 11(a) and Figure 11(b) summarizes the power plot for the full data when we
assume that blacks have better (Figure 11(a)) or worse (Figure 11(b)) mortality than whites
for both the RI and RC models. Figure 12(a) and Figure 12(b) summarize the power plot
of Q24 data when we assume the black have better (Figure 12(a)) or worse (Figure 12(b))
mortality than whites for the RI model. In the Figure 11(a) and Figure 12(a), I also plot
the vertical line of the true log Odds (B_0) for RI and RC models, respectively.

Assuming blacks have a higher mortality than whites, 80% power will be obtained for a
log OR larger than: 1) 0.13 (OR=1.139) in the RI model for the full data; 2) 0.16 (OD=1.174)
in the RC model for the full data; 3) 0.16 (OR=1.174) in the RI model for the Q24 data.
Similarly, assuming blacks have a lower mortality than whites, 80% power will be obtained
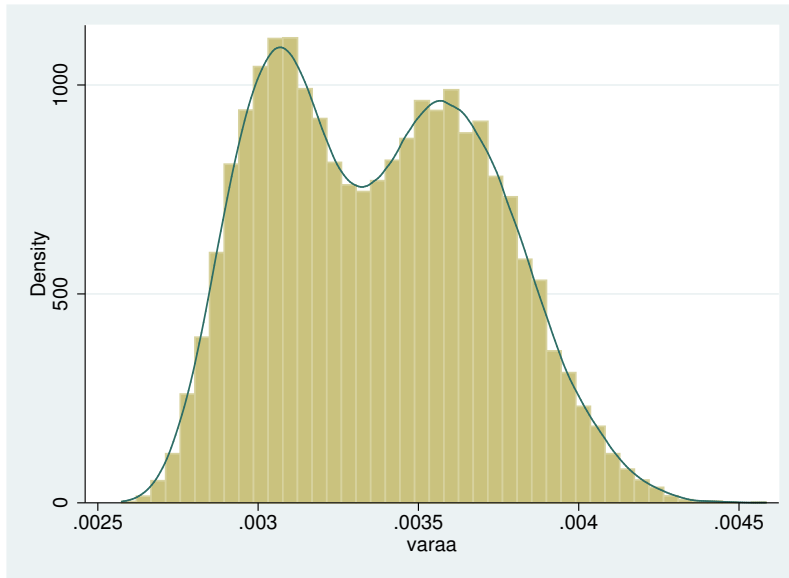
Figure IV.10: Simulated Variances of Fixed Effect for Black Race in 42 site subsample Using the RI Logistic Models (2000 iteration)

for a log OR larger than: 1) -0.14 (OR=0.869) in the RI model for the full data; 2) -0.17 (OR=0.844) in the RC model for full data; 3)-0.17 (OR=0.844) in the RI model for the Q24 data. For the same data set, the RI model has higher power to detect a specific OR. When the distribution of black patients is concentrated in the Q2-Q4 subsample, the power is somewhat lower to detect agiven OR than in the full sample. However, the sample size also is considerably smaller.
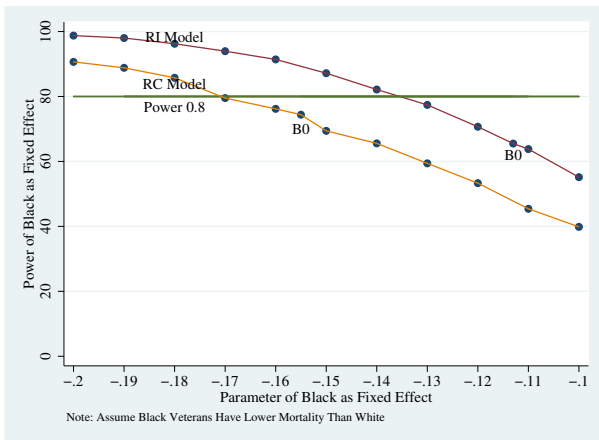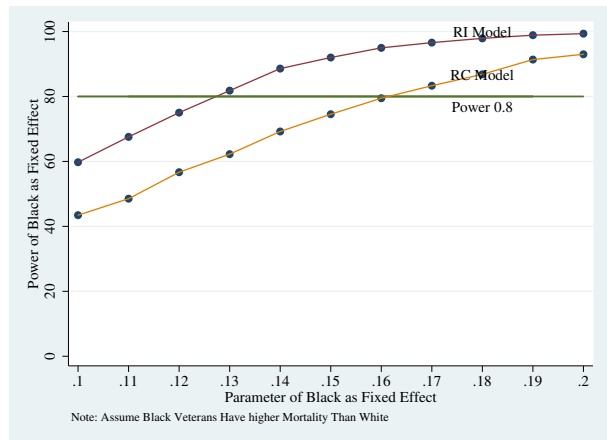
(a) Higher Mortality   (b) Lower Mortality

Figure IV.11: Log Odds Ratios that Can Be Detected with 80% Power in the RI and RC models for Veterans Younger than 65 and Hospitalized with Pneumonia, All sites
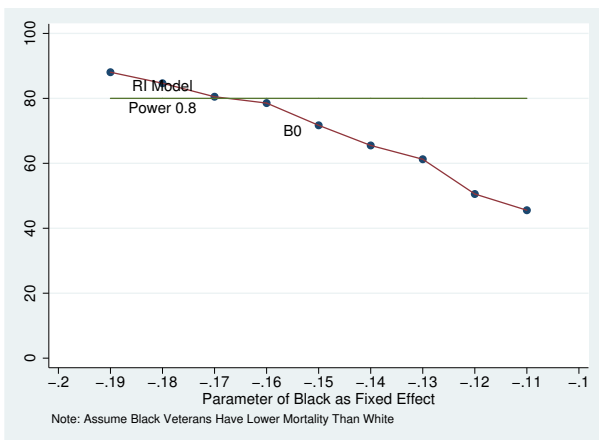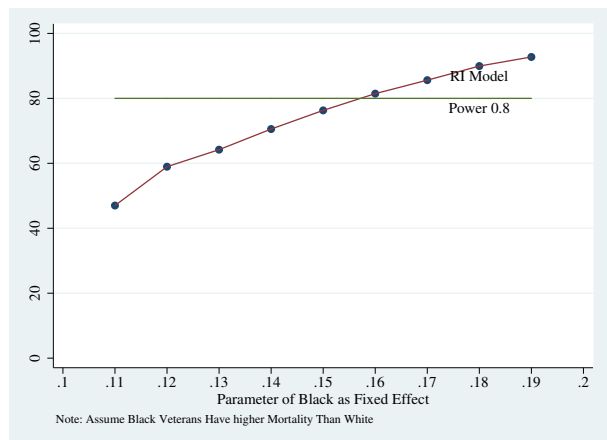
(a) Higher Mortality   (b) Lower Mortality

Figure IV.12: Log Odds Ratios that Can Be Detected with 80% Power in the RI and RC models for Veterans Younger than 65 and Hospitalized with Pneumonia for Q2Q4

V. DISCUSSION AND CONCLUSION

This dissertation focused on aspects of experimental design involving unbalanced data and two level RI and RC logistic model. I extended explicit variance formulae for a fixed effect in two level model for balanced binary data [45] to account for imbalance both between and within clusters. The same analytic variance is obtained when one has either equal numbers of observations per site and/or a constant proportion of black veterans across sites. The observed racial imbalance both within and across sites increases the variance of the race coefficient more in the RC model than in the RI model. Under a more balanced design, the analytic variances are close to the mean variance from the simulation study. Compared to PQL2, the analytic and simulated variances using MQL1 are severely downwardly biased with smaller variance components. Extending from Feiverson's algorithm[15] to estimate post-hoc power, a simulation study using the site-specific racial distributions is used to ascertain the log odds ratio for black race that can be detected with 0.80 power. The simulation variances are virtually identical to the analytic variances for these data. For a given power, somewhat smaller log odds ratios can be detected in the RI model than in the RC model.

The analytic formulae can be extended to any study using a two level logistic model without covariates and the simulation algorithm can be extended to any multilevel model. This simulation approach can be applied to design intervention studies by estimating the power of a fixed effect under different of assumed parameters and variance components.

The MCMC or MC posterior 95% CIs for a two level RI model under both balanced[77] and unbalanced[52] design can provide accurate parameter estimates, they are computationally intensive. These Bayesian approaches offer only a rough range of parameter estimates rather than specific parameter values in the two level RI model.

The RIGLS PQL2 method, although optimal within the quasi-likelihood approaches, is

biased and has convergence problems. Compared to PQL2, the analytic variances using MQL1 are severely downwardly biased with smaller variance components. In general, variance formulae derived from MQL1 are still good enough to plan an experimental design. I limited my dissertation to a two level logistic model without a covariate. Covariates have an effect on intervention through their effect on the unexplained variance. Therefore, we should take covariates into account at the design stage. MLwiN uses Goldstein's asymptotic Wald test [25] to test fixed effect and variance component. Both parameter estimation and hypothesis testing on variance components is an active research area [25][63]. Although to analytic formulae and the simulation approach are general, some of the results are specific to the imbalance structure observed in the Volpp study. In addition, very similar variance components were observed in these data, so that the analytic formulae were not that affected by differential weighting. Assessment of imbalance in other population of interest would be worthwhile.

My future work can be 1) the unbalanced design in 2-level logistic model with covariates, as an extension to the result of Moerbeek et al.[50] for balanced data with a binary covariate, 2) balanced and unbalanced design in MLLMs with more than two levels; and 3) parameter estimation and hypothesis testing on the variance components in MLLMs.

My analytic formulae demonstrates that the imbalance structure has an impact on the variance only when population are imbalance both within and across sites. These methods provide a basics for planning multilevel studies when the site-specific population structure is known. Methods that account for imbalance are particularly useful in studies of racial disparities when populations typically are highly imbalance both within and across sites.

The derived formulas provide a basis for planning multi-center studies when a predictor of primary importance is highly unbalanced both between and within sites. In studies of racial disparities in health care, the site-specific population distributions are often known from administrative data. These methods for unbalanced data may facilitate more effective planning of public health relevant multi-center studies of racial disparities.

APPENDIX A

DEFINITION OF ACRONYM

AHRQ	The Agency for Healthcare Research and Quality
AMI	Acute myocardial infarction
BDIC	Bayesian deviance information criterion
BIRLS	Beneficiary Identification Record Locator System File
CDSS	Complete-data sufficient statistics
CHERP	The Center for Health Equity Research and Promotion
CHF	Congestive heart failure
DIC	Deviance information criterion
EM	Expectation-Maximization
FML	Full maximum likelihood
GI Bleed	Gastro-intestinal bleeding
GLS	Generalized least squares
IGLS	Iterative generalized least squares
MCMC	Markov Chain Monte Carlo
MGLM	Multilevel generalized linear model
MLE	Maximum likelihood estimate
MLLM	Multilevel logistic model
MLM	Multilevel linear model
MQL	Marginal quasi-likelihood estimate

MQL1	First order of marginal quasi-likelihood estimate
MQL2	Second order of marginal quasi-likelihood estimate
NDI	National Death Index
PQL	Propensity quasi-likelihood estimate
PQL1	First order of propensity quasi-likelihood estimate
PQL2	Second order of propensity quasi-likelihood estimate
Q1	Lowest quartile of average annual black patient volume
Q2-Q4	Second to forth quartiles of average annual black patient volume
PTF	Patient Treatment File
RC	Random coefficient model
REML	Residual(or Restricted) maximum likelihood
RI	Random intercept model
RIGLS	Restricted iterative generalized least squares
VA	Veterans Affairs

APPENDIX B

GLOSSARY

Cluster	A grouping containing 'lower level' elements
Design matrix	The matrix of independent variables X and Z in the fixed or random part
Explanatory variable	In the fixed part of the model, usually denoted by x
(independent variable)	In the random part denoted by z
Fixed part	Denoted by $X\beta$, it is the average relationship
Level	A component of a data hierarchy. Level 1 is the lowest level
Level n variation	The variation of level n unit measurements about the fixed part of a model
Nesting	The clustering of units into a hierarchy
Random part	Represented by $Z\mu$ as the contribution of the random variables
Unit	An entity defined at a level of a data hierarchy

MATHEMATICAL NOTATION

Definition	Symbol
Y	Response variable vector
X	Explanatory variable design matrix
X_{ij}	Fixed part explanatory variable design matrix for a single unit in level 1
X_j	Fixed part explanatory variable design matrix for a single unit in level 2
$e_{ij} = \sum_{h=0}^{q1} e_{hij} Z_{hij}^{(1)}$	Total residuals at level 1 in a 2-level model
$\mu_j = \sum_{h=0}^{q2} \mu_{hj} Z_{hj}^{(2)}$	Total residuals at level 2 in a 2-level model
$Z^{(1)}$	Explanatory variable design matrix for level 1 random coefficients
$Z^{(2)}$	Explanatory variable design matrix for level 2 random coefficients
$\hat{y}_{ij} = X_{ij}\hat{\beta} = (X\hat{\beta})_{ij}$	Predicted value from fixed part of model
$\tilde{y}_{ij} = y_{ij} - \hat{y}_{ij}$	Raw or total residual for level 1 unit
$\tilde{y}_j = \frac{1}{n_j} \sum_{i=1}^{n_j} \hat{y}_{ij}$	Mean raw residual for level 2 unit
$\hat{\nu}_j, \hat{e}_{ij}$	Estimated residual or posterior residual estimate
$\Omega_i, \Omega = \{\Omega_i\}$	Covariance matrix of random coefficients at level i
()	Group denoting vector or matrix of elements
V_k or V	Covariance matrix of response vector for k_{th} level model
$V_{k(i)}$ or $V_{(i)}$	Contribution to covariance matrix of response vector from level i
$vec(A)$	Vec operator on matrix
$y \overset{iid}{\sim} g$	Observation(y) independently and identically

	distributed with specified density function(g)
M	Total sample size. Might written as $\sum_{j=1}^{N} \sum_{j_{i=1}}^{n} n_{ij}$ or $\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} n_{ijB} + \sum_{j=1}^{N} \sum_{i=1}^{n_{jW}} n_{ijW}$
W	White patients
t	At t_{th} iteration
t+1	At $(t + 1)_{th}$ iteration
j	Site level, $j = 1, \ldots, N$
i	Individual level, $i = 1, \ldots, n_j$
n_{jB}	Sample size for j_{th} hospital, black patients only
n_{jW}	Sample size for j_{th} hospital, white patients only
n_j	Sample size for j_{th} hospital
w_j	Site specific sample size weight
$w_{\frac{1}{2}}$	Assumed balanced weight within sites
$\bar{w}$	Assumed common weight across sites $\frac{\sum n_{jB}}{\sum n_j}$

APPENDIX D

DERIVATION OF VARIANCE OF A FIXED EFFECT FOR RACE

In this appendix, I present step by step derivations on how to extend explicit variance formulae of $var(\beta_1)$ for fixed effects in two-level balanced binary data[45][50]. This will account for the imbalance both between and within sites. I restrict the derivation of variance to a 2-level random intercept (RI) logistic model and a random coefficient (RC) logistic model without any covariate. To make the matter concrete, I will then apply this method to Volpp et al. pneumonia data[76]from a study designed to detect racical disparities in 30-day in-hospital mortality across 149 VA hospitals. The variance formulae of race [var (black)] will be presented under different design scenarios.

This data contain $M = \sum_{j=1}^{N} \sum_{i=1}^{n_j} n_{ij}$ samples, which are distributed in j $(j = 1, \ldots, N)$ hospitals, and i $(i = 1, \ldots, n_j)$ patients nested in each hospital. The binary outcome variable is $\mathbf{Y}_{ij}$ (30 days in hospital mortality), which is assumed to follow binomial distribution. π_{ij} is the probability of response proportion for the i_{th} patient in level one and j_{th} patient in level two equal to one as $\pi_{ij} = pr(\mathbf{y}_{ij} = 1)$. The link function is logit (π_{ij}) and equal to logit$(\pi_{ij}/(1 - \pi_{ij}))$. ε is the error term in the model, and n_{ij} is the denominate for the mortality. This model includes only one predictor, patient racial status (X_{ij}). Therefore, Y_{ijB} represents the death status for the i_{th} black patient at j_{th} hospital, while Y_{ijtW} refers to the death status for the i_{th}white patient at j_{th} hospital. The j_{th} hospital has n_{jB} black and n_{jW} white patients. After explaining the 2-level logistic model and linearizing the generalized multilevel linear models, I then discuss the design scenarios for unbalanced design. D.B detailed the derivation of var (black) in RI and RC models by different race coding. As

a binary variable, race can be coded as 1 and -1, or 1 and 0, for black and white veteran patients, respectively.

A.   LINEARIZATION OF A GENERALIZED LINEAR MODEL

A 2-level logistic model can usually be written as shown below (D.1).

$$
\begin{aligned}
&logit\pi_{ij} = (\mathbf{X}\beta)_{ij} + (\mathbf{Z}_\mu\mu)_j + (\mathbf{Z}_\varepsilon\varepsilon)_{ij} \\
&\text{where} \quad y_{ij} \sim BIN(\pi_{ij}, \mathbf{n_{ij}}), \qquad var(\mathbf{y}_{ij}|\pi_{ij}) = \pi_{ij}(1-\pi_{ij})/\mathbf{n}_{ij}, \\
&\mathbf{X} = [\mathbf{X}_{ij}], \quad \mathbf{X}_{ij} = \{x_{0ij}, x_{1ij}, \ldots, x_{pij}\}, \qquad Z_\varepsilon = 1 \\
&\mu_j \sim N(0, \sigma^2_{\nu_j}), \quad \text{and} \qquad \varepsilon_{ij} \sim N(0, \sigma^2_\varepsilon)
\end{aligned} \tag{D.1}
$$

This model can be written in a standard way, as a special case of a 2−level logistic model, which includes the level 1 variation (D.2).

$$
\begin{aligned}
&\mathbf{y}_{ij} = \pi_{ij} + (\mathbf{Z}_\varepsilon\varepsilon)_{ij} = f(H) + (\mathbf{Z}_\varepsilon\varepsilon)_{ij} = f((\mathbf{X}\beta)_{ij} + (\mathbf{Z}_\mu\mu)_j) + (\mathbf{Z}_\varepsilon\varepsilon)_{ij}, \\
&\text{where} \quad \mathbf{Z}_{\varepsilon ij} = \sqrt{\pi_{ij}(1-\pi_{ij})/\mathbf{n}_{ij}}, \ \sigma^2_\varepsilon = \mathbf{1}, \ \mu_j \sim N(0, \sigma^2_{\nu_j}), \\
&\text{and} \quad \pi_{\mathbf{ij}} = \mathbf{f(H)} = [\mathbf{1} + \exp(-(\mathbf{X}\beta + \mathbf{Z}_\mu\mu))]^{-\mathbf{1}}.
\end{aligned} \tag{D.2}
$$

$\mathbf{H} = logit \ \pi_{ij}$, I will get

$$
\begin{aligned}
ln\frac{\pi_{ij}}{1-\pi_{ij}} &= H \\
\frac{\pi_{ij}}{1-\pi_{ij}} &= e^H \\
1 + \frac{\pi_{ij}}{1-\pi_{ij}} &= 1 + e^H \quad \text{(add 1 on both sides)} \\
\frac{1-\pi_{ij}+\pi_{ij}}{1-\pi_{ij}} &= 1 + e^H \\
\frac{1}{1-\pi_{ij}} &= 1 + e^H \\
1 - \pi_{ij} &= (1+e^H)^{-1}
\end{aligned} \tag{D.3}
$$

$$\pi_{ij} = 1 - (1 + e^H)^{-1}$$

$$= \frac{1 + e^H - 1}{(1 + e^H)} \tag{D.4}$$

$$= \frac{e^H}{(1 + e^H)} \tag{D.5}$$

By following (D.2) and making a derivative of $\pi_{ij} = f(H)$, I will get

$$f'(H) = \pi'_{ij} \tag{D.6}$$

$$= (1 - (1 + e^H)^{-1})' \quad \text{plugin (A.4)}$$

$$= -(1 + e^H)^{-1'}$$

$$= -\frac{(-1)(1 + e^H)'}{(1 + e^H)^2}$$

$$= -\frac{(-1)e^H}{(1 + e^H)^2}$$

$$= \frac{e^H}{1 + e^H} \frac{1}{1 + e^H} \quad \text{using (A.4)}$$

$$= \pi_{ij}(1 + e^H)^{-1} \quad \text{plug in (A.3)}$$

$$= \pi_{ij}(1 - \pi_{ij}) \tag{D.7}$$

Therefore

$$f'^{-1}(H) = [f(H)(1 + e^H)^{-1}]^{-1} = f^{-1}(H)(1 + e^H)$$

$$= [\pi_{ij}(1 - \pi_{ij})]^{-1} \tag{D.8}$$

Because of the existence of link function and random effect in the multilevel logistic models, 1st order marginal quasilikelihood estimate (MQL1) is the only method that derives the variance for the fix coefficients. Before the derivation, I need to linearize the 2-level logistic model as I presented in (D.2). MQL1, as one of the quasi-likelihood estimation method , use the first order of the Taylor series expansion. The Taylor series expansion can be written as

$$f(x) \approx f(a) + f'(a)(x - a) + \frac{f''(a)(x - a)^2}{2} + \ldots + \frac{f^n(a)(x - a)^n}{n!} + \ldots$$

If I represent $f(\tilde{H}_{t+1})$ as the estimates in the $(t + 1)_{th}$ iteration, and $f(a) = f(\tilde{H}_t)$ as the estimates in the t_{th} iteration, I can get $f(\tilde{H}_{t+1})$ estimates by $f(a) = f(\tilde{H}_t)$ through the MQL1 method. In MQL1, $\tilde{\mu}_t$ is assumed to be 0, which ignores the random effect estimates.

Therefore, $\tilde{H}_t$ is $(\mathbf{X}\tilde{\beta})_{ij}$. To get the estimates at the $(t+1)_{th}$ iteration, π_{ij} can be written as below

$$
\begin{aligned}
\pi_{ij} = f(H_{t+1}) &\approx f(\tilde{H}_t) + [f(\tilde{H}_{t+1}) - f(\tilde{H}_t)]f'(\tilde{H}_t) \\
&= f(\tilde{H}_t) + [X_{ij}\beta + \mathbf{Z}_\mu\mu - (X_{ij}\tilde{\beta}_t + \mathbf{Z}_\mu\tilde{\mu_t})]f'(\tilde{H}_t) \\
&= f(\tilde{H}_t) + (X_{ij}\beta + \mathbf{Z}_\mu\mu - X_{ij}\tilde{\beta}_t)f'(\tilde{H}_t) \\
&= f(\tilde{H}_t) + (X_{ij}\beta + \mathbf{Z}_\mu\mu)f'(\tilde{H}_t) - X_{ij}\tilde{\beta}_t f'(\tilde{H}_t) \quad\quad\quad (\text{D.9})
\end{aligned}
$$

Times $f'^{(-1)}(\tilde{H}_t)$ to both side,

$$
\begin{aligned}
\pi_{ij}f'^{(-1)}(\tilde{H}_t) &= f(\tilde{H}_t)f'^{(-1)}(\tilde{H}_t) + (X_{ij}\beta + \mathbf{Z}_\mu\mu)f'(\tilde{H}_t)f'^{(-1)}(\tilde{H}_t) - X_{ij}\tilde{\beta}_t f'(\tilde{H}_t)f'^{(-1)}(\tilde{H}_t) \\
&= f(\tilde{H}_t)f'^{(-1)}(\tilde{H}_t) + X_{ij}\beta + \mathbf{Z}_\mu\mu - X_{ij}\tilde{\beta}_t
\end{aligned}
$$

Plug in (D.8) for $f'^{(-1)}(\tilde{H}_t)$

$$
\begin{aligned}
\pi_{ij}f^{-1}(\tilde{H}_t)(1 + e^{\tilde{H}}) &= f(\tilde{H}_t)f^{-1}(\tilde{H}_t)(1 + e^{\tilde{H}_t}) + X_{ij}\beta + \mathbf{Z}_\mu\mu - X_{ij}\tilde{\beta}_t \\
&= 1 + e^{\tilde{H}_t} + X_{ij}\beta + \mathbf{Z}_\mu\mu - X_{ij}\tilde{\beta}_t \quad\quad \text{plugin (A.3)} \\
&= (1 - \tilde{\pi}_{ij})^{-1} + X_{ij}\beta + \mathbf{Z}_\mu\mu - X_{ij}\tilde{\beta}_t \\
&= (1 - \tilde{\pi}_{ij})^{-1} - X_{ij}\tilde{\beta}_t + X_{ij}\beta + \mathbf{Z}_\mu\mu \quad\quad\quad (\text{D.10})
\end{aligned}
$$

If I multiply $f'^{(-1)}(\tilde{H}_t)$ with the equation $\mathbf{y}_{ij} = \pi_{ij} + (\mathbf{Z}_\varepsilon\varepsilon)_{ij}$, I get

$$
\mathbf{y}_{ij}f'^{(-1)}(\tilde{H}_t) = \pi_{ij}f'^{(-1)}(\tilde{H}_t) + (\mathbf{Z}_\varepsilon\varepsilon)_{ij}f'^{(-1)}(\tilde{H}_t)
$$

If I denote

$$
\begin{aligned}
\varepsilon^*_{ij} &= (\mathbf{Z}_\varepsilon\varepsilon)_{ij}f'^{(-1)}(\tilde{H}_t) \\
&= (\mathbf{Z}_\varepsilon\varepsilon)_{ij} * [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} \quad\quad\quad (\text{D.11})
\end{aligned}
$$

Then the results in (D.8), (D.10), (D.11) yield

$$
\mathbf{y}_{ij}[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} = (1 - \tilde{\pi}_{ij})^{-1} - X_{ij}\tilde{\beta}_t + X_{ij}\beta + \mathbf{Z}_\mu\mu + \varepsilon^*_{ij}
$$

By moving the 1st and 2nd terms on the right side to the left, I will get

$$\mathbf{y}_{ij}[\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-1} - (1-\tilde{\pi}_{ij})^{-1} + X_{ij}\tilde{\beta}_t \;=\; X_{ij}\beta + \mathbf{Z}_\mu\mu + \varepsilon_{ij}^*$$

$$(\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-1} + X_{ij}\tilde{\beta}_t \;=\; X_{ij}\beta + \mathbf{Z}_\mu\mu + \varepsilon_{ij}^*$$

If I denote

$$\mathbf{y}_{ij}^* = (\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-1} + X_{ij}\tilde{\beta}_t \tag{D.12}$$

I will then get a linearized model

$$\mathbf{y}_{ij}^* = \; X_{ij}\beta + \mathbf{Z}_\mu\mu + \varepsilon_{ij}^* \tag{D.13}$$

a). $\mathbf{var}(\varepsilon_{ij}^*)$

From the definition of the linearized logistic model, σ_ε^2 is 1. By applying this value to the linearized model, I get

$$
\begin{aligned}
\mathbf{var}(\varepsilon_{ij}^*) \;&=\; var(Z_\varepsilon\varepsilon_{ij} * [\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-1}) \\
&=\; z_\varepsilon^2[\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-2} var(\varepsilon_{ij}) \\
&=\; z_\varepsilon^2[\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-2}\sigma_\varepsilon^2 \\
&=\; z_\varepsilon^2[\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-2} \qquad \text{use } z_\varepsilon \text{ definition in model (A.2)} \\
&=\; (\sqrt{\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})/\mathbf{n}_{ij}})^2[\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-2} \\
&=\; \frac{\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})}{n_{ij}}\frac{1}{[\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^2} \\
&=\; [n_{ij}\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-1} \qquad n_{ij} \text{ is 1 in logistic model} \\
&=\; [\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-1} \tag{D.14}
\end{aligned}
$$

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Apply (D.4) to get

$$
\begin{aligned}
\mathbf{var}(\varepsilon_{ij}^*) &= [\frac{e^{X\beta}}{1+e^{X\beta}}(1-\frac{e^{X\beta}}{1+e^{X\beta}})]^{-1} \\
&= [\frac{e^{X\beta}}{1+e^{X\beta}}\frac{1+e^{X\beta}-e^{X\beta}}{1+e^{X\beta}}]^{-1} \\
&= [\frac{e^{X\beta}}{(1+e^{X\beta})^2}]^{-1} \\
&= [\frac{e^{X\beta}}{1+e^{2X\beta}+2e^{X\beta}}]^{-1} \\
&= [\frac{1}{e^{-X\beta}+e^{X\beta}+2}]^{-1} \\
&= 2+e^{-X\beta}+e^{X\beta} \qquad\qquad\qquad\qquad\qquad\qquad \text{(D.15)}
\end{aligned}
$$

b). $\mathbf{E}(\varepsilon_{ij}^*)$

$$
\begin{aligned}
\mathbf{E}(\varepsilon_{ij}^*) &= E(Z_\varepsilon \varepsilon_{ij} * [\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-1}) \\
&= E(Z_\varepsilon \varepsilon_{ij}) * [\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-1} \\
&= 0 \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad \text{(D.16)}
\end{aligned}
$$

c). $\mathbf{var}(\mathbf{Y}_{ij}^*)$

For the generalized 2-level linearized logistic model, I will get the $\mathbf{var}(\mathbf{Y}_{ij}^*)$ as

$$
\begin{aligned}
\mathbf{var}(\mathbf{Y}_{ij}^*) &= \mathbf{var}(\mathbf{X}_{ij}\beta + \mathbf{Z}_\mu \mu + \varepsilon_{ij}^*) \\
&= \mathbf{var}(\mu_j) + \mathbf{var}(\varepsilon_{ij}^*) \\
&= \mathbf{Z}_\mu' \mathbf{V}_\mu \mathbf{Z}_\mu + [\tilde{\pi}_{ij}(1-\tilde{\pi}_{ij})]^{-1} \qquad\qquad\qquad \text{(D.17)}
\end{aligned}
$$

d). $\mathbf{E}(\mathbf{Y}_{ij}^*)$

$$
\begin{aligned}
\mathbf{E(Y_{ij}^*)} &= \mathbf{E(X_{ij}\beta + Z_\mu\mu + \varepsilon_{ij}^*)} \\
&= \mathbf{E(X_{ij}\beta) + E(Z_\mu\mu) + E(\varepsilon_{ij}^*)} \\
&= X_{ij}\beta
\end{aligned}
\tag{D.18}
$$

E). $\mathbf{E(Y_{ij})}$

Obviously, Y_{ij} will follow a logistic distribution in the standard 2-level logistic model representation in model D.2. With a known mean and variance of Y_{ij}, the standard multilevel logistic distribution [45] can be normalized:

$$
\begin{aligned}
\mathbf{E(Y_{ij})} &= (\mathbf{1 + e}^{\frac{-\mathbf{X_{ij}}\beta}{\sqrt{1+\mathbf{var(Y^*)}/1.7^2}}})^{-1} \\
&\approx (\mathbf{1 + e}^{\frac{-\mathbf{X_{ij}}\beta}{\sqrt{1+\sigma_\mu^2/1.7^2}}})^{-1}
\end{aligned}
\tag{D.19}
$$

B. UNBALANCED EXPERIMENTAL DESIGN SCENARIOS

In Table III.1, I give a full list of the notation that I will used for this dissertation. The total sample size, M, is related to site-specific sample size and sample size weight. Figure D1 presents the hierarchical data structure. Because of the hierarchical structure, imbalance can occur both across and within sites.

$$
\begin{array}{ccc}
 & \overbrace{\text{Total sample size M}} & \\
\text{hospital} & 1,2,3 \quad \dots \quad j \quad \dots \quad N &
\end{array}
$$

$$
\text{At } j_{th} \text{ hospital} \qquad \overbrace{1,2,\dots,n_j}^{j}
$$

$$
\text{for black } n_{jB} \qquad\qquad \text{for white } n_{jW}
$$
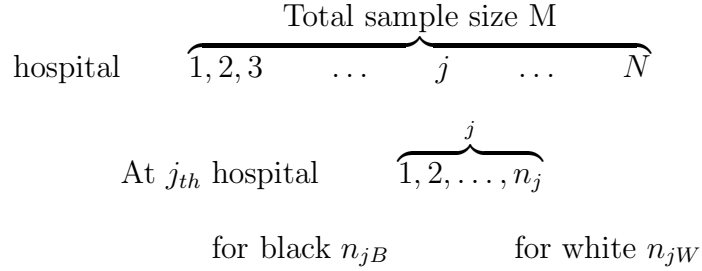
Figure D1: The Hierarchical Structure in 2-level Data

a. Balanced across sites $(n_1 = n_2 = \cdots = n_j)$

$B_{\frac{1}{2}}(w_j = \frac{1}{2})$: Balanced among sites and within sites

$B_{\bar{w}}(w_j = \bar{w})$: Balanced among sites and unbalanced within sites with same sample size weight

$B_{w_j}(w_j = w_j)$: Balanced among sites and unbalanced within sites with different sample size weight

b. Unbalanced across sites $(n_1 \neq n_2 \neq \cdots \neq n_j)$

$U_{\frac{1}{2}}(w_j = \frac{1}{2})$: Unbalanced among sites and balanced within sites

$U_{\bar{w}}(w_j = \bar{w})$: Unbalanced among and within sites with same sample size weight

$U_{w_j}(w_j = w_j)$: Unbalanced among and within sites with different sample size weight

As I mentioned, $w_j = n_{jB}/n_j$. Therefore, for general cases as scenarios B_{w_j} and U_{w_j}

$$
n_{jB} = w_j n_j \qquad \text{and} \qquad n_{jW} = (1 - w_j)n_j \tag{D.20}
$$

In special cases, $B_{\frac{1}{2}}$, $B_{\bar{w}}$, $U_{\frac{1}{2}}$, and $U_{\bar{w}}$, race-specific sample size can be simplified as

$$
\begin{aligned}
B_{\frac{1}{2}} : \quad & n_{jB} & = & \quad n/2, & \quad & n_{jW} = n/2; \\
B_{\bar{w}} : \quad & n_{jB} & = & \quad \bar{w}n, & \quad & n_{jW} = (1 - \bar{w})n; \\
U_{\frac{1}{2}} : \quad & n_{jB} & = & \quad n_j/2, & \quad & n_{jW} = n_j/2; \\
U_{\bar{w}} : \quad & n_{jB} & = & \quad \bar{w}n_j, & \quad & n_{jW} = (1 - \bar{w})n_j.
\end{aligned}
\tag{D.21}
$$

C. VERIFICATION OF MOERBEEK'S RESULT

Moerbeek et al. 2001[45] gives the formulae of $var(\beta_1)$ for a 2-level logistic model under a balanced experimental design within and across sites. Intervention is the only independent variable in the model, using 1 and -1 coding. I verify the formulae of $var(\beta_1)$ for 2-level RI and RC logistic models with one independent variable using the data from Volpp study. The formulae for $var(\beta_1)$ in a 2-level RI logistic model will be shown in D.C.1. In the following section (D.C.2), formulae for 2-level RC model will be verified.

1. Two-Level RI Logistic Model with One Independent Variable

In D.A, I showed the linearization of a generalized 2-level logistic model. Here, I will simplify the linearization to a 2-level random intercept logistic model with one independent variable(black race). As I mentioned in Section D.B, x_{ij} will denote a dichotomous variable black, which is 1 and -1 for patients who are black and white, respectively.
The random intercept model can be written as

$$\mathbf{y}_{ij} = \beta_0 + x_{ij}\beta_1 + \mu_{0j} + \varepsilon_{ij} \tag{D.22}$$

If I apply a general linearized 2-level logistic model to a 2 level random intercept model, the equation(D.13) will be modified to

$$\mathbf{y}_{ij}^* = \beta_0 + x_{ij}\beta_1 + \mu_{0j} + \varepsilon_{ij}^* \tag{D.23}$$

where, $\mathbf{y}_{ij}^*$ and ε_{ij}^* are

$$
\begin{aligned}
\mathbf{y}_{ij}^* &= (\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + x_{ij}\beta_1 \\
\varepsilon_{ij}^* &= \varepsilon_{ij}[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1}
\end{aligned}
\tag{D.24}
$$

Therefore, $\mathbf{var}(\mathbf{Y}_{ij}^*)$ for the random intercept model can be written as

$$\mathbf{var}(\mathbf{Y}_{ij}^*) = \sigma_{\mu_0}^2 + [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} \tag{D.25}$$

To identify the fixed effect of black race, I can rewrite the model (10) as

$$
\begin{aligned}
\mathbf{y}^*_{ijB} &= \beta_0 + \beta_1 + \mu_{0j} + \varepsilon^*_{ij} \quad \text{if } x_{ij} \text{ is 1 as black} \\
\mathbf{y}^*_{ijW} &= \beta_0 - \beta_1 + \mu_{0j} + \varepsilon^*_{ij} \quad \text{if } x_{ij} \text{ is -1 as white}
\end{aligned}
\tag{D.26}
$$

After applying a balanced randomization within and across hospitals, I will have 1 to J hospitals. Each hospital has n patients and half of the patients at each hospital are assumed to be black.

For black patients:

$$
\begin{aligned}
\bar{y}^*_{..B} &= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n/2} (\beta_0 + \beta_1 + \mu_{0j} + \varepsilon^*_{ijB})}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n/2} \beta_0 + \sum_{j=1}^{N} \sum_{i=1}^{n/2} \beta_1 + \sum_{j=1}^{N} \sum_{i=1}^{n/2} \mu_{0j} + \sum_{j=1}^{N} \sum_{i=1}^{n/2} \varepsilon^*_{ijB}}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{\frac{Nn}{2}\beta_0 + \frac{Nn}{2}\beta_1 + \frac{n}{2} \sum_{j=1}^{N} \mu_{0j} + \sum_{j=1}^{N} \sum_{i=1}^{n/2} \varepsilon^*_{ijB}}{\frac{Nn}{2}} \\
&= \beta_0 + \beta_1 + \frac{\sum_{j=1}^{N} \mu_{0j}}{N} + \bar{\varepsilon}^*_{..B} \\
&= \beta_0 + \beta_1 + E(\mu_{0j}) + \bar{\varepsilon}^*_{..B} \\
&= \beta_0 + \beta_1 + \bar{\varepsilon}^*_{..B}
\end{aligned}
\tag{D.27}
$$

$$
\begin{aligned}
\bar{y}^*_{.jB} &= \frac{\sum_{i=1}^{n/2} (\beta_0 + \beta_1 + \mu_{0j} + \varepsilon^*_{ijB})}{\sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{\sum_{i=1}^{n/2} \beta_0 + \sum_{i=1}^{n/2} \beta_1 + \sum_{i=1}^{\frac{n}{2}} \mu_{0j} + \sum_{i=1}^{n/2} \varepsilon^*_{ijB}}{\sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{\frac{n}{2}\beta_0 + \frac{n}{2}\beta_1 + \frac{n}{2}\mu_{0j} + \sum_{i=1}^{n/2} \varepsilon^*_{ijB}}{\frac{n}{2}} \\
&= \beta_0 + \beta_1 + \mu_{0j} + \bar{\varepsilon}^*_{.jB}
\end{aligned}
\tag{D.28}
$$

For white patients:

$$\bar{y}^*_{..W} = \frac{\sum_{j=1}^{N}\sum_{i=1}^{n/2}(\beta_0 - \beta_1 + \mu_{0j} + \varepsilon^*_{ijW})}{\sum_{j=1}^{N}\sum_{i=1}^{n/2} n_{ij}}$$

$$= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n/2}\beta_0 - \sum_{j=1}^{N}\sum_{i=1}^{n/2}\beta_1 + \sum_{j=1}^{N}\sum_{i=1}^{n/2}\mu_{0j} + \sum_{j=1}^{N}\sum_{i=1}^{n/2}\varepsilon^*_{ijW}}{\sum_{j=1}^{N}\sum_{i=1}^{n/2} n_{ij}}$$

$$= \frac{\frac{Nn}{2}\beta_0 - \frac{Nn}{2}\beta_1 + \frac{n}{2}\sum_{j=1}^{N}\mu_{0j} + \sum_{j=1}^{N}\sum_{i=1}^{n/2}\varepsilon^*_{ijW}}{\frac{Nn}{2}}$$

$$= \beta_0 - \beta_1 + \frac{\sum_{j=1}^{N}\mu_{0j}}{N} + \bar{\varepsilon}^*_{..W}$$

$$= \beta_0 - \beta_1 + \bar{\varepsilon}^*_{..W} \qquad (D.29)$$

$$\bar{y}^*_{.jW} = \frac{\sum_{i=1}^{n/2}(\beta_0 - \beta_1 + \mu_{0j} + \varepsilon^*_{ijW})}{\sum_{i=1}^{n/2} n_{ij}}$$

$$= \frac{\sum_{i=1}^{n/2}\beta_0 - \sum_{i=1}^{n/2}\beta_1 + \sum_{i=1}^{n/2}\mu_{0j} + \sum_{i=1}^{n/2}\varepsilon^*_{ijW}}{\sum_{i=1}^{n/2} n_{ij}}$$

$$= \frac{\frac{n}{2}\beta_0 - \frac{n}{2}\beta_1 + \frac{n}{2}\mu_{0j} + \sum_{i=1}^{n/2}\varepsilon^*_{ijW}}{\frac{n}{2}}$$

$$= \beta_0 - \beta_1 + \mu_{0j} + \bar{\varepsilon}^*_{.jc} \qquad (D.30)$$

By applying $\frac{(D.27)-(D.29)}{2}$ and $E(\mu_{0j}) = 0$ to (D.29), I also noticed that $E(\varepsilon^*_{ij}) = 0$, which lead to $\bar{\varepsilon}^*_{ijB} = \bar{\varepsilon}^*_{ijW} = 0$, so

$$\frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2} = \frac{\beta_0 + \beta_1 + \bar{\varepsilon}^*_{..B} - (\beta_0 - \beta_1 + \bar{\varepsilon}^*_{..W})}{2}$$

$$= \beta_1 \qquad (D.31)$$

Using the definition of Y^* in (D.24) yields

$$\mathbf{y}^*_{ij} = (\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \tilde{\beta}_0 + x_{ij}\tilde{\beta}_1$$

$$\mathbf{y}^*_{ijB} = (\mathbf{y}_{ijB} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + \beta_1 \quad \text{for black}$$

$$\mathbf{y}^*_{ijW} = (\mathbf{y}_{ijW} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 - \beta_1 \quad \text{for white} \qquad (D.32)$$

I can write $\mathbf{E}(\mathbf{y}^*_{ijB})$ and $\mathbf{E}(\mathbf{y}^*_{ijW})$ as

$$
\begin{aligned}
\mathbf{E}(\mathbf{y}^*_{ijB}) &= \mathbf{E}\{(\mathbf{y}_{ijB} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + \beta_1 \\
&= (\mathbf{E}(\mathbf{y}_{ijB}) - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + \beta_1
\end{aligned}
$$

$$
\begin{aligned}
\mathbf{E}(\bar{\mathbf{y}}^*_{..B}) &= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n/2} E(y_{ijB})}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n/2} E(\mathbf{y}_{ijB} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} + \beta_0 + \beta_1}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n/2} E(\mathbf{y}_{ijB} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} + \sum_{j=1}^{N} \sum_{i=1}^{n/2} (\beta_0 + \beta_1)}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{E(\sum_{j=1}^{N} \sum_{i=1}^{n/2} \mathbf{y}_{ijB} - \sum_{j=1}^{N} \sum_{i=1}^{n/2} \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ij})]^{-1} + \sum_{j=1}^{N} \sum_{i=1}^{n/2} (\beta_0 + \beta_1)}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= (E\bar{y}_{..B} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} + \beta_0 + \beta_1
\end{aligned}
$$

$$
\begin{aligned}
E(\bar{y}^*_{..W}) &= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n/2} E(y_{ijW})}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n/2} E(\mathbf{y}_{ijW} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1} + \beta_0 + \beta_1}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n/2} E(\mathbf{y}_{ijW} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1} + \sum_{j=1}^{N} \sum_{i=1}^{n/2} (\beta_0 + \beta_1)}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= \frac{E(\sum_{j=1}^{N} \sum_{i=1}^{n/2} \mathbf{y}_{ijW} - \sum_{j=1}^{N} \sum_{i=1}^{n/2} \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ij})]^{-1} + \sum_{j=1}^{N} \sum_{i=1}^{n/2} (\beta_0 + \beta_1)}{\sum_{j=1}^{N} \sum_{i=1}^{n/2} n_{ij}} \\
&= (E\bar{y}_{..W} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1} + \beta_0 - \beta_1 \quad\quad (\text{D.33})
\end{aligned}
$$

By applying (D.33) to (D.31), I will get $E(\beta_1)$ as

$$
\begin{aligned}
E(\beta_1) &= E\frac{(\bar{y}^*_{..B} - \bar{y}^*_{..W})}{2} \\
&= \frac{E\bar{y}^*_{..B} - E\bar{y}^*_{..W}}{2} \\
&= \frac{(E\bar{y}_{..B} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} + \beta_0 + \beta_1 - \{(E\bar{y}_{..W} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1} + \beta_0 - \beta_1\}}{2} \\
&= \frac{2\beta_1 + (E\bar{y}_{..B} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} - (E\bar{y}_{..W} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1}}{2} \\
&= \frac{2\beta_1 + (Ey_{ijB} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} - (Ey_{ijW} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1}}{2} \quad\quad (\text{D.34})
\end{aligned}
$$

By following the approximate normalization of y in the logistic distribution as I showed in (D.19) and adapting it to the random intercept model, I get $E(Y_{ijB})$ and $E(Y_{ijW})$ as

$$
\begin{aligned}
\mathbf{E}(\mathbf{Y_{ijB}}) &= (\mathbf{1}+\mathbf{e}^{\frac{-\mathbf{x_{ij}}\beta}{\sqrt{1+\sigma_\mu^2/1.7^2}}})^{-\mathbf{1}} \\
&= (\mathbf{1}+\mathbf{e}^{\frac{-(\beta_0+\beta_1)}{\sqrt{1+\sigma_{\mu_0}^2/1.7^2}}})^{-\mathbf{1}} \quad \text{denote} \sqrt{1+\sigma_{\mu_0}^2/1.7^2} = c \\
&= [\mathbf{1}+\mathbf{e}^{\frac{-(\beta_0+\beta_1)}{c}}]^{-\mathbf{1}}
\end{aligned}
$$

$$
\begin{aligned}
\mathbf{E}(\mathbf{Y_{ijW}}) &= (\mathbf{1}+\mathbf{e}^{\frac{-\mathbf{x_{ij}}\beta}{\sqrt{1+\sigma_\mu^2/1.7^2}}})^{-\mathbf{1}} \\
&= (\mathbf{1}+\mathbf{e}^{\frac{-(\beta_0-\beta_1)}{\sqrt{1+\sigma_{\mu_0}^2/1.7^2}}})^{-\mathbf{1}} \quad \text{denote} \sqrt{1+\sigma_{\mu_0}^2/1.7^2} = c \\
&= [\mathbf{1}+\mathbf{e}^{\frac{-(\beta_0-\beta_1)}{c}}]^{-\mathbf{1}} \tag{D.35}
\end{aligned}
$$

Modifying (D.15) to black and white effect yields

$$
\begin{aligned}
\mathbf{var}(\varepsilon^*_{\mathbf{ij}}) &= 2 + e^{-x\beta} + e^{x\beta} \\
\text{So} \quad \mathbf{var}(\varepsilon^*_{\mathbf{ijB}}) &= 2 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1} \quad \text{for Black} \\
\mathbf{var}(\varepsilon^*_{\mathbf{ijW}}) &= 2 + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1} \quad \text{for White} \tag{D.36}
\end{aligned}
$$

Adapting (D.4) results in π_{ijB} and π_{ijW} as

$$
\begin{aligned}
\pi_{ij} &= 1 - (1 + e^H)^{-1} \\
\pi_{ijB} &= 1 - (1 + e^{\beta_0+\beta_1})^{-1} \quad \text{for Black} \\
\pi_{ijW} &= 1 - (1 + e^{\beta_0-\beta_1})^{-1} \quad \text{for White} \tag{D.37}
\end{aligned}
$$

By following (D.34), I can write $E(\beta_1)$ as

$$
\begin{aligned}
E(\beta_1) &= \beta_1 + \frac{1}{2}(2 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1})\{[\mathbf{1}+\mathbf{e}^{\frac{-(\beta_0+\beta_1)}{c}}]^{-1} - (1 + e^{\beta_0+\beta_1})^{-1}\} \\
&\quad - \frac{1}{2}(2 + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1})\{[\mathbf{1}+\mathbf{e}^{\frac{-(\beta_0-\beta_1)}{c}}]^{-1} - (1 + e^{\beta_0-\beta_1})^{-1}\} \tag{D.38}
\end{aligned}
$$

$$
\begin{aligned}
var(\beta_1) &= var(\frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2}) \\[2ex]
&= var(\frac{\frac{\sum_j^N \bar{y}^*_{.jB}}{N} - \frac{\sum_j^N \bar{y}^*_{.jW}}{N}}{2}) \\[2ex]
&= var\{\frac{1}{2N}(\sum_{j=1}^N (\beta_0 + \beta_1 + \mu_{0j} + \bar{\varepsilon}^*_{.jB}) - \sum_{j=1}^N (\beta_0 - \beta_1 + \mu_{0j} + \bar{\varepsilon}^*_{.jc})\} \\[2ex]
&= var\{\frac{1}{2N}[(N\beta_0 + N\beta_1 + \sum_{j=1}^N \mu_{0j}) + \sum_{j=1}^N \bar{\varepsilon}^*_{.jB} - (N\beta_0 - N\beta_1 + \sum_{j=1}^N \mu_{0j} + \sum_{j=1}^N \bar{\varepsilon}^*_{.jc})]\} \\[2ex]
&= var\{\frac{1}{2N}(2N\beta_1 + \sum_{j=1}^N \bar{\varepsilon}^*_{.jB} - \sum_{j=1}^N \bar{\varepsilon}^*_{.jc})\} \\[2ex]
&= var\{\beta_1 + \frac{1}{2N\frac{n}{2}}(\sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} \varepsilon^*_{ijB} - \sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} \varepsilon^*_{ijW})\} \\[2ex]
&= \frac{1}{(Nn)^2} var(\sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} \varepsilon^*_{ijB} - \sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} \varepsilon^*_{ijW})) \\[2ex]
&= \frac{1}{(Nn)^2}(\sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} var\varepsilon^*_{ijB} + \sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} var\varepsilon^*_{ijW})) \\[2ex]
&= \frac{1}{(Nn)^2}[\frac{Nn}{2}(2 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1}) + \frac{Nn}{2}(2 + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1})] \\[2ex]
&= \frac{1}{(Nn)^2}\frac{nN}{2}[(2 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1}) + (2 + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1})] \\[2ex]
&= \frac{1}{2Nn}(4 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1} + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1}) \\[2ex]
&\text{let} \quad \frac{1}{2}(4 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1} + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1}) = \delta^2 \quad \text{I will get} \\[2ex]
var(\beta_1) &= \frac{\delta^2}{Nn} \quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad \text{(D.39)}
\end{aligned}
$$

2. Two-Level RC Logistic Model with One Independent Variable

The 2-level RC model can be written as

$$\mathbf{y}_{ij} = \beta_0 + x_{ij}\beta_1 + \mu_0 + x_{ij}\mu_{1j} + \varepsilon_{ij} \tag{D.40}$$

If I apply a general linearized 2-level logistic model to 2 level random slope model, the equation(D.13) will be modified to

$$\mathbf{y}_{ij}^* = \beta_0 + x_{ij}\beta_1 + \mu_0 + x_{ij}\mu_{1j} + \varepsilon_{ij}^* \tag{D.41}$$

By applying (D.12) and (D.11) to this model, $\mathbf{y}_{ij}^*$ and ε_{ij}^* will be

$$
\begin{aligned}
\mathbf{y}_{ij}^* &= (\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \tilde{\beta}_0 + x_{ij}\tilde{\beta}_1 \\
\varepsilon_{ij}^* &= \varepsilon_{ij}[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1}
\end{aligned}
\tag{D.42}
$$

After applying (D.17) to random slope model, $\mathbf{var}(\mathbf{Y}_{ij}^*)$ can be written as

$$\mathbf{var}(\mathbf{Y}_{ij}^*) = \sigma_{\mu_0}^2 + \sigma_{\mu_1}^2 + [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} \tag{D.43}$$

To identify the fixed effect of black race, I can rewrite the model () as

$$
\begin{aligned}
\mathbf{y}_{ijB}^* &= \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ij}^* \quad \text{if } x_{ij} \text{ is 1 as black} \\
\mathbf{y}_{ijW}^* &= \beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \varepsilon_{ij}^* \quad \text{if } x_{ij} \text{ is -1 as white}
\end{aligned}
\tag{D.44}
$$

I then apply a balanced randomization within and across 1 to J hospitals, which have n patients in each hospital of whom half are black.

For black patients:

$$\bar{y}^*_{.jB} = \frac{\sum_{i=1}^{n/2}(\beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon^*_{ijB})}{n_{jB}}$$

$$= \frac{\sum_{i=1}^{n/2}\beta_0 + \sum_{i=1}^{n/2}\beta_1 + \sum_{i=1}^{n/2}\mu_{0j} + \sum_{i=1}^{n/2}\mu_{1j} + \sum_{i=1}^{n/2}\varepsilon^*_{ijB}}{\frac{n}{2}}$$

$$= \frac{\frac{n}{2}\beta_0 + \frac{n}{2}\beta_1 + \frac{n}{2}\mu_{0j} + \frac{n}{2}\mu_{1j} + \sum_{i=1}^{n/2}\varepsilon^*_{ijB}}{\frac{n}{2}}$$

$$= \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \bar{\varepsilon}^*_{.jB}$$

$$\bar{y}^*_{..B} = \frac{\sum_{j=1}^{N}\{\beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \bar{\varepsilon}^*_{.jB}\}}{N}$$

$$= \beta_0 - \beta_1 + \frac{\sum_{j=1}^{N}\mu_{0j}}{N} - \frac{\sum_{j=1}^{N}\mu_{1j}}{N} + \bar{\varepsilon}^*_{.jB}$$

$$= \beta_0 - \beta_1 + E(\mu_{0j}) - E(\mu_{1j}) + \bar{\varepsilon}^*_{.jB} \qquad \text{where} \qquad E(\mu_{0j}) = E(\mu_{0j}) = 0$$

$$= \beta_0 - \beta_1 + \bar{\varepsilon}^*_{.jB} \qquad\qquad (D.45)$$

For white patients:

$$\bar{y}^*_{.jW} = \frac{\sum_{i=1}^{n/2}(\beta_0 + \beta_1 + \mu_{0j} - \mu_{1j} + \varepsilon^*_{ijW})}{n_{jW}}$$

$$= \frac{\sum_{i=1}^{n/2}\beta_0 - \sum_{i=1}^{n/2}\beta_1 + \sum_{i=1}^{n/2}\mu_{0j} - \sum_{i=1}^{n/2}\mu_{1j} + \sum_{i=1}^{n/2}\varepsilon^*_{ijW}}{\frac{n}{2}}$$

$$= \frac{\frac{n}{2}\beta_0 - \frac{n}{2}\beta_1 + \frac{n}{2}\mu_{0j} - \frac{n}{2}\mu_{1j} + \sum_{i=1}^{n/2}\varepsilon^*_{ijW}}{\frac{n}{2}}$$

$$= \beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \bar{\varepsilon}^*_{.jW}$$

$$\bar{y}^*_{..W} = \frac{\sum_{j=1}^{N}\{\beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \bar{\varepsilon}^*_{.jW}\}}{N}$$

$$= \beta_0 - \beta_1 + \frac{\sum_{j=1}^{N}\mu_{0j}}{N} - \frac{\sum_{j=1}^{N}\mu_{1j}}{N} + \bar{\varepsilon}^*_{.jW}$$

$$= \beta_0 - \beta_1 + E(\mu_{0j}) - E(\mu_{1j}) + \bar{\varepsilon}^*_{.jW} \qquad \text{where} \qquad E(\mu_{0j}) = E(\mu_{0j}) = 0$$

$$= \beta_0 - \beta_1 + \bar{\varepsilon}^*_{.jW} \qquad\qquad (D.46)$$

Apply $\frac{(D.45)-(D.46)}{2}$ and $E(\varepsilon^*_{ij}) = 0$ (or $\bar{\varepsilon}^*_{ijB} = \bar{\varepsilon}^*_{ijW} = 0$), I will get

$$\frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2} = \frac{\beta_0 + \beta_1 + \bar{\varepsilon}^*_{ijB} - (\beta_0 - \beta_1 + \bar{\varepsilon}^*_{ijW})}{2}$$

$$= \beta_1 \qquad\qquad (D.47)$$

Following the definition of Y^* in (D.12)

$$
\begin{aligned}
\mathbf{y}_{ij}^* &= (\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \tilde{\beta}_0 + x_{ij}\tilde{\beta}_1 \\
\mathbf{y}_{ijB}^* &= (\mathbf{y}_{ijB} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + \beta_1 \quad \text{for black} \\
\mathbf{y}_{ijW}^* &= (\mathbf{y}_{ijW} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 - \beta_1 \quad \text{for white} \quad \text{(D.48)}
\end{aligned}
$$

Therefore, I can write $\mathbf{E}(\mathbf{y_{ijB}^*})$ and $\mathbf{E}(\mathbf{y_{ijW}^*})$ as

$$
\begin{aligned}
\mathbf{E}(\mathbf{y}_{ijB}^*) &= \mathbf{E}\{(\mathbf{y}_{ijB} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + \beta_1 \\
&= (\mathbf{E}(\mathbf{y}_{ijB}) - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + \beta_1
\end{aligned}
$$

$$
\begin{aligned}
\mathbf{E}(\bar{\mathbf{y}}_{..B}^*) &= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n/2} E(y_{ijB})}{\sum_{j=1}^{N}\sum_{i=1}^{n/2} n_{ijB}} \\
&= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n/2} E(\mathbf{y}_{ijB} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} + \beta_0 + \beta_1}{\sum_{j=1}^{N}\sum_{i=1}^{n/2} n_{ijB}} \\
&= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n/2} E\{(\mathbf{y}_{ijB} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} + \sum_{j=1}^{N}\sum_{i=1}^{n/2}(\beta_0 + \beta_1)\}}{\sum_{j=1}^{N}\sum_{i=1}^{n/2} n_{ijB}} \\
&= \frac{(E\sum_{j=1}^{N}\sum_{i=1}^{n/2} \mathbf{y}_{ijB} - \sum_{j=1}^{N}\sum_{i=1}^{n/2} \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ij})]^{-1} + \sum_{j=1}^{N}\sum_{i=1}^{n/2}(\beta_0 + \beta_1)}{\sum_{j=1}^{N}\sum_{i=1}^{n/2} n_{ijB}} \\
&= (E\bar{y}_{..B} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} + \beta_0 + \beta_1 \\
E(\bar{y}_{..W}^*) &= (E\bar{y}_{..W} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1} + \beta_0 - \beta_1 \quad \text{(D.49)}
\end{aligned}
$$

Applying (D.49) to (D.42) produces $E(\beta_1)$ as

$$
\begin{aligned}
E(\beta_1) &= E\frac{(\bar{y}_{..B}^* - \bar{y}_{..W}^*)}{2} \\
&= \frac{E\bar{y}_{..B}^* - E\bar{y}_{..W}^*}{2} \\
&= \frac{(E\bar{y}_{..B} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} + \beta_0 + \beta_1 - \{E\bar{y}_{..W} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1} + \beta_0 - \beta_1\}}{2} \\
&= \frac{2\beta_1 + (E\bar{y}_{..B} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} - (E\bar{y}_{..W} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1}}{2} \\
&= \frac{2\beta_1 + (Ey_{ijB} - \tilde{\pi}_{ijB})[\tilde{\pi}_{ijB}(1 - \tilde{\pi}_{ijB})]^{-1} - (Ey_{ijW} - \tilde{\pi}_{ijW})[\tilde{\pi}_{ijW}(1 - \tilde{\pi}_{ijW})]^{-1}}{2} \quad \text{(D.50)}
\end{aligned}
$$

Following an approximate normalization of y in the logistic distribution, $E(y_{ij})$ as shown in (D.19), I will get modified $E(Y_{ijB})$ and $E(Y_{ijW})$ in the random slope model as

$$
\begin{aligned}
\mathbf{E(Y_{ijB})} &= (\mathbf{1+e}^{\frac{-\mathbf{x_{ij}}\beta}{\sqrt{\mathbf{1+(\sigma_\mu^2+\sigma_{\mu_1}^2)/1.7^2}}}})^{-\mathbf{1}} \\
&= (\mathbf{1+e}^{\frac{-(\beta_0+\beta_1)}{\sqrt{\mathbf{1+(\sigma_{\mu_0}^2+\sigma_{\mu_1}^2)/1.7^2}}}})^{-\mathbf{1}} \\
&= [\mathbf{1+e}^{\frac{-(\beta_0+\beta_1)}{\mathbf{c}}}]^{-\mathbf{1}}
\end{aligned}
$$

$$
\begin{aligned}
\mathbf{E(Y_{ijW})} &= (\mathbf{1+e}^{\frac{-(\beta_0-\beta_1)}{\sqrt{\mathbf{1+(\sigma_{\mu_0}^2+\sigma_{\mu_1}^2)/1.7^2}}}})^{-\mathbf{1}} \\
&= [\mathbf{1+e}^{\frac{-(\beta_0-\beta_1)}{\mathbf{c}}}]^{-\mathbf{1}} \quad\quad (\text{D.51})
\end{aligned}
$$

Applying (D.13) to black and white effect, I will get

$$
\begin{aligned}
[\tilde{\pi}_{ijB}(1-\tilde{\pi}_{ijB})]^{-1} &= 2 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1} \quad\quad \text{Black} \\
\{\tilde{\pi}_{ijW}(1-\tilde{\pi}_{ijW})\}^{-1} &= 2 + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1} \quad\quad \text{White} \quad\quad (\text{D.52})
\end{aligned}
$$

Modifying (D.4) results in π_{ijB} and π_{ijW} as

$$
\begin{aligned}
\pi_{ij} &= 1 - (1+e^H)^{-1} \\
\pi_{ijB} &= 1 - (1+e^{\beta_0+\beta_1})^{-1} \quad\quad \text{Black} \\
\pi_{ijW} &= 1 - (1+e^{\beta_0-\beta_1})^{-1} \quad\quad \text{White} \quad\quad (\text{D.53})
\end{aligned}
$$

Using a GLS of $\hat{\beta}_1 = \frac{y_{..B}-y_{..W}}{2}$ as (D.47), I can write $E(\beta_1)$ as

$$
\begin{aligned}
E(\beta_1) &= \beta_1 + \frac{1}{2}(2 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1})\{[\mathbf{1+e}^{\frac{-(\beta_0+\beta_1)}{\mathbf{c}}}]^{-1} - (1+e^{\beta_0+\beta_1})^{-1}\} \\
&\quad - \frac{1}{2}(2 + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1})\{[\mathbf{1+e}^{\frac{-(\beta_0-\beta_1)}{\mathbf{c}}}]^{-1} - (1+e^{\beta_0-\beta_1})^{-1}\} \quad (\text{D.54})
\end{aligned}
$$

$$\begin{aligned}
var(\beta_1) &= var(\frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2}) \\
&= var(\frac{\frac{\sum_j^N \bar{y}^*_{.jB}}{N} - \frac{\sum_j^N \bar{y}^*_{.jW}}{N}}{2}) \qquad \text{apply (D.45), (D.46)} \\
&= var\{\frac{1}{2N}(\sum_{j=1}^N (\beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \bar{\varepsilon}^*_{.jB}) \\
&\quad - \sum_{j=1}^N (\beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \bar{\varepsilon}^*_{.jW})\} \\
&= var\{\frac{1}{2N}(N\beta_0 + N\beta_1 + \sum_{j=1}^N \mu_{0j} - \sum_{j=1}^N \mu_{1j}) \\
&\quad + \sum_{j=1}^N \bar{\varepsilon}^*_{.jB} - (N\beta_0 - N\beta_1 + \sum_{j=1}^N \mu_{0j} - \sum_{j=1}^N \mu_{1j} + \sum_{j=1}^N \bar{\varepsilon}^*_{.jW})\} \\
&= var\{\frac{1}{2N}(2N\beta_1 + 2\sum_{j=1}^N \mu_{1j} + \sum_{j=1}^N \bar{\varepsilon}^*_{.jB} - \sum_{j=1}^N \bar{\varepsilon}^*_{.jW})\} \\
&= var\{\beta_1 + \frac{\sum_{j=1}^N \mu_{1j}}{N} + \frac{1}{2N\frac{n}{2}}(\sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} \varepsilon^*_{ijB} - \sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} \varepsilon^*_{ijW})\} \\
&= \frac{N\sigma^2_{\mu_1}}{N^2} + \frac{1}{(Nn)^2} var(\sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} \varepsilon^*_{ijB} - \sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} \varepsilon^*_{ijW}) \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{1}{(Nn)^2}(\sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} var\varepsilon^*_{ijB} + \sum_{j=1}^N \sum_{i=1}^{\frac{n}{2}} var\varepsilon^*_{ijW}) \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{1}{(Nn)^2}[\frac{nN}{2}(2 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1}) + \frac{nN}{2}(2 + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1})] \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{1}{(Nn)^2}\frac{nN}{2}[(2 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1}) + (2 + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1})] \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{1}{2Nn}(4 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1} + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1}) \\
&\quad \text{let} \quad \frac{1}{2}(4 + e^{-(\beta_0+\beta_1)} + e^{\beta_0+\beta_1} + e^{-(\beta_0-\beta_1)} + e^{\beta_0-\beta_1}) = \delta^2 \quad \text{I will get}
\end{aligned}$$

$$\begin{aligned}
var(\beta_1) &= \frac{\sigma^2_{\mu_1}}{N} + \frac{\delta^2}{Nn} \\
&= \frac{n\sigma^2_{\mu_1} + \delta^2}{Nn} \qquad\qquad\qquad\qquad\qquad\qquad \text{(D.55)}
\end{aligned}$$

D. $VAR(\beta_1)$ **UNDER AN UNBALANCED DESIGN**

As I mentioned at the beginning of this appendix, the binary variable of race can be described by two types of coding: 1 and -1, and 1 and 0. Under these codings, the models have different interpretations and different results for $var(\beta_1)$. The next subsection, Appendix D.D.1, will introduce the derivation for 1 and -1 coding. While the follow subsection D.D.2will present the derivation on 1 and 0 coding. Both codings first show the derivation as the RI model and then the RC model derivation.

1. $var(\beta_1)$ **For Zero Sum Coding**

Here, I present the derivation of $var(\beta_1)$ under six design scenarios for the RI model and RC model when I code race as 1 for black and -1 for white. I will apply the formulae as shown in D.C to D.D.1. No matter how the independent variables are coded, the multilevel generalized linear model's linearization is the same as (D.13). In this section, I will derive variance of race which is coded as 1 for black and -1 for white veterans. The same unbalance design scenarios as discussed in D.D.2 will be considered here.

a. **In RI Model**

Adapting the general linearized to the 2-level logistic model (D.13) to the 2-level RI model adjusted by one binary variable and coded as 1 and -1 for black and white, yields the following results

$$\mathbf{y}_{ij}^* = \beta_0 + x_{ij}\beta_1 + \mu_{0j} + \varepsilon_{ij}^* \tag{D.56}$$

To identify the black effect, I can rewrite the model (D.14) as the race specific models

$$
\begin{aligned}
\mathbf{y}_{ijB}^* &= \beta_0 + \beta_1 + \mu_{0j} + \varepsilon_{ij}^* && \text{for black} \\
\mathbf{y}_{ijW}^* &= \beta_0 - \beta_1 + \mu_{0j} + \varepsilon_{ij}^* && \text{for white}
\end{aligned}
\tag{D.57}
$$

Therefore, the age linearized race specific responses at j_{th} site are shown as (D.58) and (D.59) for black and white respectively.

$$
\begin{aligned}
\bar{y}^*_{.jB} &= \frac{\sum_{i=1}^{n_{jB}} (\beta_0 + \beta_1 + \mu_{0j} + \varepsilon^*_{ijB})}{n_{jB}} \qquad \text{for black} \\
&= \frac{\sum_{i=1}^{n_{jB}} (\beta_0) + \sum_{i=1}^{n_{jB}} (\beta_1) + \sum_{i=1}^{n_{jB}} (\mu_{0j}) + \sum_{i=1}^{n_{jB}} (\varepsilon^*_{ijB})}{n_{jB}} \\
&= \frac{n_{jB}\beta_0 + n_{jB}\beta_1 + n_{jB}\mu_{0j} + \sum_{i=1}^{n_{jB}} (\varepsilon^*_{ijB})}{n_{jB}} \\
&= \beta_0 + \beta_1 + \mu_{0j} + \bar{\varepsilon}^*_{.jB} \qquad (E\varepsilon^*_{.jB} = 0) \\
&= \beta_0 + \beta_1 + \mu_{0j} \qquad\qquad\qquad\qquad\qquad (\text{D.58})
\end{aligned}
$$

$$
\begin{aligned}
\bar{y}^*_{.jw} &= \frac{\sum_{i=1}^{n_{jW}} (\beta_0 - \beta_1 + \mu_{0j} + \varepsilon^*_{ijW})}{\sum_{i=1}^{n_{jW}} 1} \qquad \text{for white} \\
&= \frac{\sum_{i=1}^{n_{jW}} (\beta_0) - \sum_{i=1}^{n_{jW}} (\beta_1) + \sum_{i=1}^{n_{jW}} (\mu_{0j}) + \sum_{i=1}^{n_{jW}} (\varepsilon^*_{ijW})}{n_{jW}} \\
&= \frac{n_{jW}\beta_0 - n_{jW}\beta_1 + n_{jW}\mu_{0j} + \sum_{i=1}^{n_{jW}} (\varepsilon^*_{ijW})}{n_{jW}} \\
&= \beta_0 - \beta_1 + \mu_{0j} + \bar{\varepsilon}^*_{.jW} \qquad (E\varepsilon^*_{.jW} = 0) \\
&= \beta_0 - \beta_1 + \mu_{0j} \qquad\qquad\qquad\qquad\qquad (\text{D.59})
\end{aligned}
$$

Similarly, we can get average outcome as shown below.

$$
\begin{aligned}
\bar{y}^*_{..B} &= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\beta_0 + \beta_1 + \mu_{0j} + \varepsilon^*_{ijB})}{\sum_{j=1}^{N} n_{jB}} \qquad\qquad\qquad \text{for black} \\
&= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\beta_0) + \sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\beta_1) + \sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\mu_{0j}) + \sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\varepsilon^*_{ijB})}{n_B} \\
&= \frac{n_B\beta_0 + n_B\beta_1 + \sum_{j=1}^{N} n_{jB}\mu_{0j} + \sum_{i=1}^{n_{jB}} \sum_{j=1}^{N} (\varepsilon^*_{ijB})}{n_B} \\
&= \beta_0 + \beta_1 + \frac{\sum_{j=1}^{N} n_{jB}\mu_{0j}}{n_B} + \bar{\varepsilon}^*_{..B} \\
&= \beta_0 + \beta_1 + \bar{\mu}_{0B} + \bar{\varepsilon}^*_{..B} \qquad (E\mu_0 = 0) \\
&= \beta_0 + \beta_1 \qquad\qquad\qquad\qquad\qquad\qquad (\text{D.60})
\end{aligned}
$$

$$\bar{y}^*_{..W} = \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\beta_0 - \beta_1 + \mu_{0j} + \varepsilon^*_{ijW})}{\sum_{j=1}^{N} n_{jW}} \qquad \text{for white}$$

$$= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\beta_0) - \sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\beta_1) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\mu_{0j}) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\varepsilon^*_{ijW})}{n_W}$$

$$= \frac{n_W\beta_0 - n_W\beta_1 + \sum_{j=1}^{N} n_{jW}\mu_{0j} + \sum_{i=1}^{n_{jW}}\sum_{j=1}^{N}(\varepsilon^*_{ijW})}{n_W}$$

$$= \beta_0 - \beta_1 + \frac{\sum_{j=1}^{N} n_{jW}\mu_{0j}}{n_W} + \bar{\varepsilon}^*_{..W}$$

$$= \beta_0 - \beta_1 + \bar{\mu}_{0W} + \bar{\varepsilon}^*_{..W} \qquad (E\mu_0 = 0)$$

$$= \beta_0 - \beta_1 \tag{D.61}$$

Therefore, the generalized least squares(GLS) estimate of race can be obtained by

$$\bar{y}^*_{..B} - \bar{y}^*_{..W} = \beta_0 + \beta_1 - \beta_0 - \beta_1 = 2\beta_1$$

$$\text{so} \qquad \hat{\beta}_1 = \frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2} \tag{D.62}$$

Applying corresponded f(H) to (D.12) and (D.11), the modified $\mathbf{y}^*_{ij}$ and ε^*_{ij} result in

$$\mathbf{y}^*_{ij} = (\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + x_{ij}\beta_1$$

$$\varepsilon^*_{ij} = \varepsilon_{ij}[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} \tag{D.63}$$

Then, applying $V_j = \sigma^2_{\mu_0}$ to $\mathbf{var}(\mathbf{Y}^*_{ij})$ as (D.17) for RI model yields

$$\mathbf{var}(\mathbf{Y}^*_{ij}) = \sigma^2_{\mu_0} + [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} \tag{D.64}$$

Based on the linearized 2-level logistic model (D.13) and the applied GLS estimate of β_1 as (D.62), I get

$$\hat{\beta}_1 = \frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2}$$

$$= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}} y^*_{ijB} - \sum_{j=1}^{N}\sum_{i=1}^{n_{jB}} y^*_{ijW}}{2}$$

$$= \frac{\sum_{j=1}^{N}\frac{\sum_{i=1}^{n_{jB}}\{\beta_0+\beta_1+\mu_{0j}+\varepsilon^*_{ij}\}}{n_{jB}} - \sum_{j=1}^{N}\frac{\sum_{i=1}^{n_{jW}}\{\beta_0-\beta_1+\mu_{0j}+\varepsilon^*_{ij}\}}{n_{jW}}}{2N} \tag{D.65}$$

β_0 and β_1 will be constant everywhere. μ_{0j} will be constant at j_{th} hospital.

$$
\begin{aligned}
\hat{\beta}_1 &= \frac{\frac{\sum_{j=1}^{N}(\frac{n_{jB}}{n_jB}\beta_0+\frac{n_{jB}}{n_jB}\beta_1)}{N} + \frac{\sum_{j=1}^{N}\frac{n_{jb}}{n_{jb}}\mu_{0j}}{N} + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}\varepsilon_{ijW}^*}{\sum_{j=1}^{N}n_{jB}}}{2} \\
&\quad - \frac{\frac{\sum_{j=1}^{N}(\frac{n_{jW}}{n_{jW}}\beta_0-\frac{n_{jW}}{n_{jW}}\beta_1)}{N} + \frac{\sum_{j=1}^{N}\mu_{0j}}{N} + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}\varepsilon_{ijW}^*}{\sum_{j=1}^{N}n_{jW}}}{2} \\
&= \frac{\beta_0+\beta_1+\frac{\sum_{j=1}^{N}\mu_{0j}}{N}+\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}\varepsilon_{ijB}^*}{\sum_{j=1}^{N}n_{jB}} - (\beta_0-\beta_1+\frac{\sum_{j=1}^{N}\mu_{0j}}{N}+\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}\varepsilon_{ijW}^*}{\sum_{j=1}^{N}n_{jW}})}{2} \\
&= \beta_1 + \frac{\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}\varepsilon_{ijB}^*}{\sum_{j=1}^{N}n_{jB}} - \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}\varepsilon_{ijW}^*}{\sum_{j=1}^{N}n_{jW}}}{2} \quad (\text{D.66})
\end{aligned}
$$

By applying the variance to both sides of (D.66) and the known variance of constant as 0, I will get

$$
var(\hat{\beta}_1) = \frac{var\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}\varepsilon_{ijB}^*}{\sum_{j=1}^{N}n_{jB}} + var\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}\varepsilon_{ijW}^*}{\sum_{j=1}^{N}n_{jW}}}{4}
$$

$var(\varepsilon_{ijB}^*)$ or $var(\varepsilon_{ijW}^*)$ are the same as $\sigma_{\varepsilon_{ijB}}^{2*}$ and $\sigma_{\varepsilon_{ijW}}^{2*}$ for different sites and individual combinations, respectively. I can write the above equation as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{(\sum_{j=1}^{N}n_{jB})\sigma_{\varepsilon_{ijB}}^{2*}}{(\sum_{j=1}^{N}n_{jB})^2} + \frac{(\sum_{j=1}^{N}n_{jW})\sigma_{\varepsilon_{ijW}}^{2*}}{(\sum_{j=1}^{N}n_{jW})^2}}{4} \\
var(\hat{\beta}_1) &= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N}n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N}n_{jW}}}{4} \quad (\text{D.67})
\end{aligned}
$$

For condition $B_{\frac{1}{2}}$: From (D.20), I known that $\sum_{j=1}^{N}n_{ijB} = \sum_{j=1}^{N}n_{ijW} = \frac{M}{2}$

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}}}{4} \\
var(\hat{\beta}_1) &= \frac{\frac{1}{2}(\sigma_{\varepsilon_{ijB}}^{2*} + \sigma_{\varepsilon_{ijW}}^{2*})}{M} \\
var(\beta_1) &= \frac{\delta^2}{M} \quad (\text{D.68})
\end{aligned}
$$

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For condition $B_{\bar{w}}$: $n_1 = n_2 = \cdots = n_j = n$ and $w_j = \bar{w} \neq \frac{1}{2}$, and using equation (D.21), I get

$$\sum_{j=1}^{N} n_{jB} = \bar{w}M$$

$$\sum_{j=1}^{N} n_{jW} = (1-\bar{w})M, \qquad (D.69)$$

I can write (D.67) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
&= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\bar{w}M} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{(1-\bar{w})M}}{4} \\
&= \frac{(1-\bar{w})\sigma_{\varepsilon_{ijB}}^{2*} + \bar{w}\sigma_{\varepsilon_{ijW}}^{2*}}{4\bar{w}(1-\bar{w})M} \qquad (D.70)
\end{aligned}
$$

For condition B_{w_j}: $n_1 = n_2 = \cdots = n_j = n$ and $w_j = w_j$ and by using equation (D.21), I get

$$\sum_{j=1}^{N} n_{jB} = \sum_{j=1}^{N} w_j n_j = n \sum_{j=1}^{N} w_j$$

$$\sum_{j=1}^{N} n_{jW} = \sum_{j=1}^{N} (1-w_j) n_j = n \sum_{j=1}^{N} (1-w_j), \qquad (D.71)$$

I can write (D.67) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
&= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{n \sum_{j=1}^{N} w_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{n \sum_{j=1}^{N} (1-w_j)}}{4} \\
&= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{n \sum_{j=1}^{N} w_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{n(N - \sum_{j=1}^{N} w_j)}}{4} \\
&= \frac{(N - \sum_{j=1}^{N} w_j)\sigma_{\varepsilon_{ijB}}^{2*} + \sum_{j=1}^{N} w_j \sigma_{\varepsilon_{ijW}}^{2*}}{4n(N - \sum_{j=1}^{N} w_j) \sum_{j=1}^{N} w_j} \qquad (D.72)
\end{aligned}
$$

For condition $U_{\frac{1}{2}}$: $n_1 \neq n_2 \neq \cdots \neq n_j$, $w_j = 1/2$, and $n_{jB} = n_{jW} = \frac{n_j}{2}$. Therefore,

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \sum_{j=1}^{N} \frac{1}{2} n_j = \frac{1}{2} \sum_{j=1}^{N} n_j = \frac{M}{2} \\
\sum_{j=1}^{N} n_{jW} &= \sum_{j=1}^{N} \frac{1}{2} n_j = \frac{1}{2} \sum_{j=1}^{N} n_j = \frac{M}{2}
\end{aligned}
$$

(D.73)

I can write (D.67) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
var(\hat{\beta}_1) &= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}}}{4} \\
var(\hat{\beta}_1) &= \frac{\frac{1}{2}(\sigma_{\varepsilon_{ijB}}^{2*} + \sigma_{\varepsilon_{ijW}}^{2*})}{M} \\
var(\beta_1) &= \frac{\delta^2}{M}
\end{aligned}
$$

(D.74)

For condition $U_{\bar{w}}$: $n_1 \neq n_2 \neq \cdots \neq n_j$, $w_j = \bar{w} \neq \frac{1}{2}$.

Using the following equation (D.21), I can get

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \sum_{j=1}^{N} \bar{w} n_j = \bar{w} \sum_{j=1}^{N} n_j = \bar{w} M \\
\sum_{j=1}^{N} n_{jW} &= \sum_{j=1}^{N} (1 - \bar{w}) n_j = (1 - \bar{w}) \sum_{j=1}^{N} n_j = (1 - \bar{w}) M
\end{aligned}
$$

(D.75)

This equation (D.67) can be written as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
&= \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\bar{w} M} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{(1 - \bar{w}) M}}{4} \\
&= \frac{(1 - \bar{w}) \sigma_{\varepsilon_{ijB}}^{2*} + \bar{w} \sigma_{\varepsilon_{ijW}}^{2*}}{4 \bar{w}(1 - \bar{w}) M}
\end{aligned}
$$

(D.76)

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For condition U_{w_j}: $n_1 \neq n_2 \neq \cdots \neq n_j$, $w_j = w_j$.

The following equation (D.21)produces

$$
\sum_{j=1}^{N} n_{jB} = \sum_{j=1}^{N} w_j n_j
$$

$$
\sum_{j=1}^{N} n_{jW} = \sum_{j=1}^{N} (1 - w_j) n_j, \tag{D.77}
$$

I can write (D.67) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\dfrac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \dfrac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}}}{4} \\[2ex]
&= \frac{\dfrac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} w_j n_j} + \dfrac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} (1-w_j) n_j}}{4} \\[2ex]
&= \frac{\dfrac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} w_j n_j} + \dfrac{\sigma_{\varepsilon_{ijW}}^{2*}}{(\sum_{j=1}^{N} n_j - \sum_{j=1}^{N} w_j n_j)}}{4} \\[2ex]
&= \frac{\dfrac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} w_j n_j} + \dfrac{\sigma_{\varepsilon_{ijW}}^{2*}}{M - \sum_{j=1}^{N} w_j n_j}}{4} \\[2ex]
&= \frac{(M - \sum_{j=1}^{N} w_j n_j) \sigma_{\varepsilon_{ijB}}^{2*} + (\sum_{j=1}^{N} w_j n_j) \sigma_{\varepsilon_{ijW}}^{2*}}{4(M - \sum_{j=1}^{N} w_j n_j) \sum_{j=1}^{N} w_j n_j} \tag{D.78}
\end{aligned}
$$

b. In RC Model

Adapting the general linearized 2-level logistic model (D.13) to the 2-level RC model, adjusted by race and coded as 1 and -1 for black and white, yields the following result

$$\mathbf{y}_{ij}^* = \beta_0 + x_{ij}\beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ij}^* \tag{D.79}$$

To identify the black effect, I can rewrite the model (D.14) as the race specific models

$$
\begin{aligned}
\mathbf{y}_{ijA}^* &= \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ij}^* \quad \text{for black} \\
\mathbf{y}_{ijW}^* &= \beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \varepsilon_{ij}^* \qquad \text{for white}
\end{aligned}
\tag{D.80}
$$

Therefore, the average linearized race specific response at j_{th} site are shown as (D.81) and (D.82) for black and white, respectively.

$$
\begin{aligned}
\bar{y}_{.jB}^* &= \frac{\sum_{i=1}^{n_{jB}} (\beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ijB}^*)}{n_{jB}} \qquad\qquad \text{for black} \\
&= \frac{\sum_{i=1}^{n_{jB}}(\beta_0) + \sum_{i=1}^{n_{jB}}(\beta_1) + \sum_{i=1}^{n_{jB}}(\mu_{0j}) + \sum_{i=1}^{n_{jB}}(\mu_{1j}) + \sum_{i=1}^{n_{jB}}(\varepsilon_{ijB}^*)}{n_{jB}} \\
&= \frac{n_{jB}\beta_0 + n_{jB}\beta_1 + n_{jB}\mu_{0j} + n_{jB}\mu_{1j} + \sum_{i=1}^{n_{jB}}(\varepsilon_{ijB}^*)}{n_{jB}} \\
&= \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \bar{\varepsilon}_{.jB}^* \qquad (E\varepsilon_{.jB}^* = 0) \\
&= \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} \tag{D.81}
\end{aligned}
$$

$$
\begin{aligned}
\bar{y}_{.jw}^* &= \frac{\sum_{i=1}^{n_{jW}} (\beta_0 - \beta_1 + \mu_{0j} + \varepsilon_{ijW}^*)}{\sum_{i=1}^{n_{jW}} 1} \qquad\qquad \text{for white} \\
&= \frac{\sum_{i=1}^{n_{jW}}(\beta_0) - \sum_{i=1}^{n_{jW}}(\beta_1) + \sum_{i=1}^{n_{jW}}(\mu_{0j}) + \sum_{i=1}^{n_{jW}}(\varepsilon_{ijW}^*)}{n_{jW}} \\
&= \frac{n_{jW}\beta_0 - n_{jW}\beta_1 + n_{jW}\mu_{0j} + \sum_{i=1}^{n_{jW}}(\varepsilon_{ijW}^*)}{n_{jW}} \\
&= \beta_0 - \beta_1 + \mu_{0j} + \bar{\varepsilon}_{.jW}^* \qquad (E\varepsilon_{.jW}^* = 0) \\
&= \beta_0 - \beta_1 + \mu_{0j} \tag{D.82}
\end{aligned}
$$

Similarly, the following showns the average outcome:

$$
\begin{aligned}
\bar{y}^*_{..B} &= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon^*_{ijB})}{\sum_{j=1}^{N} n_{jB}} && \text{for black} \\
&= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\beta_0) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\beta_1) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\mu_{0j}) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\mu_{1j}) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\varepsilon^*_{ijB})}{n_B} \\
&= \frac{n_B\beta_0 + n_B\beta_1 + \sum_{j=1}^{N} n_{jB}\mu_{0j} + \sum_{j=1}^{N} n_{jB}\mu_{1j} + \sum_{i=1}^{n_{jB}}\sum_{j=1}^{N}(\varepsilon^*_{ijB})}{n_B} \\
&= \beta_0 + \beta_1 + \frac{\sum_{j=1}^{N} n_{jB}\mu_{0j}}{n_B} + \frac{\sum_{j=1}^{N} n_{jB}\mu_{1j}}{n_B} + \bar{\varepsilon}^*_{..B} \\
&= \beta_0 + \beta_1 + \bar{\mu}_{0B} + \bar{\mu}_{1B} + \bar{\varepsilon}^*_{..B} && (E\mu_0 = 0 \quad \& \quad E\mu_1 = 0) \\
&= \beta_0 + \beta_1 && (\text{D.83})
\end{aligned}
$$

$$
\begin{aligned}
\bar{y}^*_{..W} &= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\beta_0 - \beta_1 + \mu_{0j} + \varepsilon^*_{ijW})}{\sum_{j=1}^{N} n_{jW}} && \text{for white} \\
&= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\beta_0) - \sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\beta_1) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\mu_{0j}) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\varepsilon^*_{ijW})}{n_W} \\
&= \frac{n_W\beta_0 - n_W\beta_1 + \sum_{j=1}^{N} n_{jW}\mu_{0j} + \sum_{i=1}^{n_{jW}}\sum_{j=1}^{N}(\varepsilon^*_{ijW})}{n_W} \\
&= \beta_0 - \beta_1 + \frac{\sum_{j=1}^{N} n_{jW}\mu_{0j}}{n_W} + \bar{\varepsilon}^*_{..W} \\
&= \beta_0 - \beta_1 + \bar{\mu}_{0W} + \bar{\varepsilon}^*_{..W} && (E\mu_0 = 0 \quad \& \quad E\mu_1 = 0) \\
&= \beta_0 - \beta_1 && (\text{D.84})
\end{aligned}
$$

Therefore, the GLS estimate of race can be obtained by

$$
\begin{aligned}
\bar{y}^*_{..B} - \bar{y}^*_{..W} &= \beta_0 + \beta_1 - \beta_0 - \beta_1 = 2\beta_1 \\
\text{So} \qquad \beta_1 &= \frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2} && (\text{D.85})
\end{aligned}
$$

Applying corresponded f(H) to (D.12) and (D.11), the modified $\mathbf{y}^*_{ij}$ and ε^*_{ij} result as

$$
\begin{aligned}
\mathbf{y}^*_{ij} &= (\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + x_{ij}\beta_1 \\
\varepsilon^*_{ij} &= \varepsilon_{ij}[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} && (\text{D.86})
\end{aligned}
$$

Then, applying $V_j = \sigma^2_{\mu_0}$ to $\mathbf{var(Y^*_{ij})}$ as (D.17) for RI model yields

$$\mathbf{var(Y^*_{ij})} \;=\; \sigma^2_{\mu_0} + \sigma^2_{\mu_1} + [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} \tag{D.87}$$

Based on the linearized 2-level logistic model (D.13) and applied GLS estimate of β_1 as (D.85), I get

$$
\begin{aligned}
\hat{\beta}_1 &= \frac{\bar{y}^*_{..B} - \bar{y}^*_{..W}}{2} \\
&= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jA}} y^*_{ijB} - \sum_{j=1}^{N} \sum_{i=1}^{n_{jA}} y^*_{ijW}}{2} \\
&= \frac{\sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} \{\beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon^*_{ij}\}}{n_{jB}} - \sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jW}} \{\beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \varepsilon^*_{ij}\}}{n_{jW}}}{2N}
\end{aligned}
\tag{D.88}
$$

As known, β_0 and β_1 will be constant as parameter estimates within the RC model. μ_{0j} and μ_{1j} will be constant in the same j_{th} hospital.

$$
\begin{aligned}
\hat{\beta}_1 &= \frac{\frac{\sum_{j=1}^{N}(\frac{n_jB}{n_jB}\beta_0 + \frac{n_jB}{n_jB}\beta_1)}{N} + \frac{\sum_{j=1}^{N}\frac{n_{jb}}{n_{jb}}\mu_{0j}}{N} + \frac{\sum_{j=1}^{N}\frac{n_{jb}}{n_{jb}}\mu_{1j}}{N} + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}\varepsilon^*_{ijW}}{\sum_{j=1}^{N}n_{jB}}}{2} \\
&\quad - \frac{\frac{\sum_{j=1}^{N}(\frac{n_jB}{n_jB}\beta_0 - \frac{n_jB}{n_jB}\beta_1)}{N} + \frac{\sum_{j=1}^{N}\frac{n_{jb}}{n_{jb}}\mu_{0j}}{N} - \frac{\sum_{j=1}^{N}\frac{n_{jb}}{n_{jb}}\mu_{1j}}{N} + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}\varepsilon^*_{ijW}}{\sum_{j=1}^{N}n_{jW}}}{2} \\
&= \frac{\beta_0 + \beta_1 + \frac{\sum_{j=1}^{N}\mu_{0j}}{N} + \frac{\sum_{j=1}^{N}\mu_{1j}}{N} + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}\varepsilon^*_{ijB}}{\sum_{j=1}^{N}n_{jB}}}{2} \\
&\quad - \frac{(\beta_0 - \beta_1 + \frac{\sum_{j=1}^{N}\mu_{0j}}{N} - \frac{\sum_{j=1}^{N}\mu_{1j}}{N} + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}\varepsilon^*_{ijW}}{\sum_{j=1}^{N}n_{jW}})}{2} \\
&= \frac{\beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}\varepsilon^*_{ijB}}{\sum_{j=1}^{N}n_{jB}}}{2} \\
&\quad - \frac{(\beta_0 - \beta_1 + \mu_{0j} - \mu_{1j} + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}\varepsilon^*_{ijW}}{\sum_{j=1}^{N}n_{jW}})}{2} \\
&= \beta_1 + \mu_{1j} + \frac{\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}\varepsilon^*_{ijB}}{\sum_{j=1}^{N}n_{jB}} - \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}\varepsilon^*_{ijW}}{\sum_{j=1}^{N}n_{jW}}}{2}
\end{aligned}
\tag{D.89}
$$

Because the variance of constant terms are o and μ_{1j} in the same across sites, the above formula results in

$$var(\hat{\beta}_1) \;\;=\;\; var\left(\frac{\sum_{j=1}^{N}\mu_{1j}}{N}\right) + \frac{var\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jA}}\varepsilon_{ijA}^{*}}{\sum_{j=1}^{N}n_{jA}} + var\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}\varepsilon_{ijW}^{*}}{\sum_{j=1}^{N}n_{jW}}}{4}$$

$var(\varepsilon_{ijA}^{*})$ or $var(\varepsilon_{ijW}^{*})$ are the same as $\sigma_{\varepsilon_{ijA}}^{2*}$ and $\sigma_{\varepsilon_{ijW}}^{2*}$ in different cells, respectively. At the same time, $var(\mu_{1j}) = \sigma_{\mu_1}^{2}$ in any site. I can write the above equation as

$$var(\hat{\beta}_1) \;\;=\;\; \frac{N\sigma_{\mu_1}^{2}}{N^2} + \frac{\frac{(\sum_{j=1}^{N}n_{jB})\sigma_{\varepsilon_{ijB}}^{2*}}{(\sum_{j=1}^{N}n_{jB})^2} + \frac{(\sum_{j=1}^{N}n_{jW})\sigma_{\varepsilon_{ijW}}^{2*}}{(\sum_{j=1}^{N}n_{jW})^2}}{4}$$

$$var(\hat{\beta}_1) \;\;=\;\; \frac{\sigma_{\mu_1}^{2}}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N}n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N}n_{jW}}}{4} \tag{D.90}$$

For condition $B_{\frac{1}{2}}$: $n_1 = n_2 = \cdots = n_j = n$, and $\sum_{j=1}^{N}n_{ijB} = \sum_{j=1}^{N}n_{ijW} = \frac{M}{2}$ Applying (D.85), this results in

$$var(\hat{\beta}_1) \;\;=\;\; \frac{\sigma_{\mu_1}^{2}}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}}}{4}$$

$$var(\hat{\beta}_1) \;\;=\;\; \frac{\sigma_{\mu_1}^{2}}{N} + \frac{\frac{1}{2}(\sigma_{\varepsilon_{ijB}}^{2*} + \sigma_{\varepsilon_{ijW}}^{2*})}{M}$$

$$var(\beta_1) \;\;=\;\; \frac{\sigma_{\mu_1}^{2}n + \delta^2}{M} \tag{D.91}$$

For condition $B_{\bar{w}}$: $n_1 = n_2 = \cdots = n_j = n$ and $w_j = \bar{w} \neq \frac{1}{2}$, applying (D.20), I can obtain

$$\sum_{j=1}^{N}n_{jB} \;\;=\;\; \bar{w}M$$

$$\sum_{j=1}^{N}n_{jW} \;\;=\;\; (1-\bar{w})nN = (1-\bar{w})M \tag{D.92}$$

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I can write (D.85) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\mu_1}^2}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\bar{w}M} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{(1-\bar{w})M}}{4} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{(1-\bar{w})\sigma_{\varepsilon_{ijB}}^{2*} + \bar{w}\sigma_{\varepsilon_{ijW}}^{2*}}{4\bar{w}(1-\bar{w})M}
\end{aligned}
\tag{D.93}
$$

For condition B_{w_j}: $n_1 = n_2 = \cdots = n_j = n$ and $w_j = w_j$, using equation (D.20), results in

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= n\sum_{j=1}^{N} w_j \\
\sum_{j=1}^{N} n_{jW} &= n\sum_{j=1}^{N}(1 - w_j),
\end{aligned}
\tag{D.94}
$$

I can write (D.85) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\mu_1}^2}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{n\sum_{j=1}^{N} w_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{n\sum_{j=1}^{N}(1-w_j)}}{4} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{n\sum_{j=1}^{N} w_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{n(N-\sum_{j=1}^{N} w_j)}}{4} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{(N - \sum_{j=1}^{N} w_j)\sigma_{\varepsilon_{ijB}}^{2*} + \sum_{j=1}^{N} w_j\sigma_{\varepsilon_{ijW}}^{2*}}{4n(N - \sum_{j=1}^{N} w_j)\sum_{j=1}^{N} w_j}
\end{aligned}
\tag{D.95}
$$

For condition $U_{\frac{1}{2}}$: $n_1 \neq n_2 \neq \cdots \neq n_j$, $w_j = 1$, and $n_{jB} = n_{jW} = \frac{n_j}{2}$ Using (D.20), the race specific sample size yields to

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \frac{M}{2} \\
\sum_{j=1}^{N} n_{jW} &= \frac{M}{2}
\end{aligned}
\tag{D.96}
$$

I can write (D.85) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma^2_{\mu_1}}{N} + \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
var(\hat{\beta}_1) &= \frac{\sigma^2_{\mu_1}}{N} + \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\frac{M}{2}} + \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\frac{M}{2}}}{4} \\
var(\hat{\beta}_1) &= \frac{\sigma^2_{\mu_1}}{N} + \frac{\frac{1}{2}\left(\sigma^{2*}_{\varepsilon_{ijB}} + \sigma^{2*}_{\varepsilon_{ijW}}\right)}{M} \\
var(\hat{\beta}_1) &= \frac{\sigma^2_{\mu_1}}{N} + \frac{\delta^2}{M}
\end{aligned}
\tag{D.97}
$$

For condition $U_{\bar{w}}$: $n_1 \neq n_2 \neq \cdots \neq n_j$, $w_j = \bar{w}$

Using the results in equation (D.21) yields

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \bar{w}M \\
\sum_{j=1}^{N} n_{jW} &= (1 - \bar{w})M
\end{aligned}
\tag{D.98}
$$

The equation (D.85) can be written as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma^2_{\mu_1}}{N} + \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} n_{jW}}}{4} \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{\frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\bar{w}M} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{(1-\bar{w})M}}{4} \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{(1 - \bar{w})\sigma^{2*}_{\varepsilon_{ijB}} + \bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{4\bar{w}(1 - \bar{w})M}
\end{aligned}
\tag{D.99}
$$

For condition U_{w_j}: $n_1 \neq n_2 \neq \cdots \neq n_j$, $w_j = w_j$. Using equation (D.21) achieves

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \sum_{j=1}^{N} w_j n_j \\
\sum_{j=1}^{N} n_{jW} &= \sum_{j=1}^{N} (1 - w_j) n_j,
\end{aligned}
\tag{D.100}
$$

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I can write (D.85) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\mu_1}^2}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^N n_{jW}}}{4} \\[2ex]
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N w_j n_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^N (1-w_j) n_j}}{4} \\[2ex]
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N w_j n_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{(\sum_{j=1}^N n_j - \sum_{j=1}^N w_j n_j)}}{4} \\[2ex]
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N w_j n_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{M - \sum_{j=1}^N w_j n_j}}{4} \\[2ex]
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{(M - \sum_{j=1}^N w_j n_j)\sigma_{\varepsilon_{ijB}}^{2*} + (\sum_{j=1}^N w_j n_j)\sigma_{\varepsilon_{ijW}}^{2*}}{4(M - \sum_{j=1}^N w_j n_j)\sum_{j=1}^N w_j n_j}
\end{aligned}
\tag{D.101}
$$

2. $var(\beta_1)$ For "Reference Level" Coding

No matter how the independent variables are coded, the multilevel generalized linear model's linearization is the same as (D.13). In this section, I will derive the variance of race which is coded as 1 for black and 0 for white veterans. The same unbalance design scenarios as discussed in Appendix D.D.2 will be considered, here.

a. In RI Model

Adapting the general linearized 2-level logistic model (D.13) to the 2 level RI model, adjusted by one binary variable and coded as 1 in black and 0 for white race, yields the following results:

$$\mathbf{y}_{ij}^* = \beta_0 + x_{ij}\beta_1 + \mu_{0j} + \varepsilon_{ij}^* \tag{D.102}$$

To identify the black effect, I can rewrite the model (D.14) as the race specific models

$$
\begin{aligned}
\mathbf{y}_{ijA}^* &= \beta_0 + \beta_1 + \mu_{0j} + \varepsilon_{ij}^* \quad \text{for black} \\
\mathbf{y}_{ijW}^* &= \beta_0 + \mu_{0j} + \varepsilon_{ij}^* \qquad \text{for white}
\end{aligned}
\tag{D.103}
$$

Therefore, the average linearized race specific response at j_{th} site are shown as (D.104) and (D.105) for black and white, respectively.

$$
\begin{aligned}
\bar{y}_{.jB}^* &= \frac{\sum_{i=1}^{n_{jB}}(\beta_0 + \beta_1 + \mu_{0j} + \varepsilon_{ijB}^*)}{n_{jB}} \qquad \text{for black} \\
&= \frac{\sum_{i=1}^{n_{jB}}(\beta_0) + \sum_{i=1}^{n_{jB}}(\beta_1) + \sum_{i=1}^{n_{jB}}(\mu_{0j}) + \sum_{i=1}^{n_{jB}}(\varepsilon_{ijB}^*)}{n_{jB}} \\
&= \frac{n_{jB}\beta_0 + n_{jB}\beta_1 + n_{jB}\mu_{0j} + \sum_{i=1}^{n_{jB}}(\varepsilon_{ijB}^*)}{n_{jB}} \\
&= \beta_0 + \beta_1 + \mu_{0j} + \bar{\varepsilon}_{.jB}^* \qquad (E\varepsilon_{.jB}^* = 0) \\
&= \beta_0 + \beta_1 + \mu_{0j}
\end{aligned}
$$

$$\tag{D.104}$$

$$
\begin{aligned}
\bar{y}^*_{.jw} &= \frac{\sum_{i=1}^{n_{jW}} (\beta_0 + \mu_{0j} + \varepsilon^*_{ijW})}{\sum_{i=1}^{n_{jW}} 1} \qquad \text{for white} \\
&= \frac{\sum_{i=1}^{n_{jW}} (\beta_0) + \sum_{i=1}^{n_{jW}} (\mu_{0j}) + \sum_{i=1}^{n_{jW}} (\varepsilon^*_{ijW})}{n_{jW}} \\
&= \frac{n_{jW}\beta_0 + n_{jW}\mu_{0j} + \sum_{i=1}^{n_{jW}} (\varepsilon^*_{ijW})}{n_{jW}} \\
&= \beta_0 + \mu_{0j} + \bar{\varepsilon}^*_{.jW} \qquad (E\varepsilon^*_{.jW} = 0) \\
&= \beta_0 + \mu_{0j} \tag{D.105}
\end{aligned}
$$

Similarly, we can get an average outcome as shown below.

$$
\begin{aligned}
\bar{y}^*_{..B} &= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\beta_0 + \beta_1 + \mu_{0j} + \varepsilon^*_{ijB})}{\sum_{j=1}^{N} n_{jB}} \qquad \text{for black} \\
&= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\beta_0) + \sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\beta_1) + \sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\mu_{0j}) + \sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} (\varepsilon^*_{ijB})}{n_B} \\
&= \frac{n_B\beta_0 + n_B\beta_1 + \sum_{j=1}^{N} n_{jB}\mu_{0j} + \sum_{i=1}^{n_{jB}} \sum_{j=1}^{N} (\varepsilon^*_{ijB})}{n_B} \\
&= \beta_0 + \beta_1 + \frac{\sum_{j=1}^{N} n_{jB}\mu_{0j}}{n_B} + \bar{\varepsilon}^*_{..B} \\
&= \beta_0 + \beta_1 + \bar{\mu}_{0B} + \bar{\varepsilon}^*_{..B} \qquad (E\mu_0 = 0) \\
&= \beta_0 + \beta_1 \tag{D.106}
\end{aligned}
$$

$$
\begin{aligned}
\bar{y}^*_{..W} &= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jW}} (\beta_0 + \mu_{0j} + \varepsilon^*_{ijW})}{\sum_{j=1}^{N} n_{jW}} \qquad \text{for white} \\
&= \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jW}} (\beta_0) + \sum_{j=1}^{N} \sum_{i=1}^{n_{jW}} (\mu_{0j}) + \sum_{j=1}^{N} \sum_{i=1}^{n_{jW}} (\varepsilon^*_{ijW})}{n_W} \\
&= \frac{n_W\beta_0 + \sum_{j=1}^{N} n_{jW}\mu_{0j} + \sum_{i=1}^{n_{jW}} \sum_{j=1}^{N} (\varepsilon^*_{ijW})}{n_W} \\
&= \beta_0 + \frac{\sum_{j=1}^{N} n_{jW}\mu_{0j}}{n_W} + \bar{\varepsilon}^*_{..W} \\
&= \beta_0 + \bar{\mu}_{0W} + \bar{\varepsilon}^*_{..W} \qquad (E\mu_0 = 0) \\
&= \beta_0 \tag{D.107}
\end{aligned}
$$

Therefore, the GLS estimate of race can be obtained by

$$
\bar{y}^*_{..B} - \bar{y}^*_{..W} = \beta_0 + \beta_1 - \beta_0 = \beta_1 \tag{D.108}
$$

By applying the corresponding f(H) to (D.12) and (D.11), the modified $\mathbf{y}^*_{ij}$ and ε^*_{ij} results in

$$
\begin{aligned}
\mathbf{y}^*_{ij} &= (\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + x_{ij}\beta_1 \\
\varepsilon^*_{ij} &= \varepsilon_{ij}[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1}
\end{aligned}
\tag{D.109}
$$

Then, applying $V_j = \sigma^2_{\mu_0}$ to $\mathbf{var(Y^*_{ij})}$ as (D.17) for RI model yields

$$
\mathbf{var(Y^*_{ij})} = \sigma^2_{\mu_0} + [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1}
\tag{D.110}
$$

Based on the linearized 2-level logistic model (D.13) and by applying the GLS estimate of β_1 as (D.108), I get

$$
\begin{aligned}
\hat{\beta}_1 &= \bar{y}^*_{..B} - \bar{y}^*_{..W} \\
\hat{\beta}_1 &= \frac{\sum_{j=1}^{N} \bar{y}^*_{.jB} - \sum_{j=1}^{N} \bar{y}^*_{.jW}}{N} \\
\hat{\beta}_1 &= \frac{\sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} y^*_{ijB}}{n_{jB}} - \sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jW}} y^*_{ijW}}{n_{jW}}}{N}
\end{aligned}
\tag{D.111}
$$

I have presented y_{ijB} and y_{ijW} as (D.103). Plugging in (D.111), I will get

$$
\hat{\beta}_1 = \frac{\sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} \{\beta_0 + \beta_1 + \mu_{0j} + \varepsilon^*_{ij}\}}{n_{jB}} - \sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} \{\beta_0 + \mu_{0j} + \varepsilon^*_{ij}\}}{n_{jW}}}{N}
$$

β_0 and β_1 will be constant everywhere.

$$
\begin{aligned}
\hat{\beta}_1 &= \beta_0 + \beta_1 + \mu_0 + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}} \varepsilon^*_{ijB}}{\sum_{j=1}^{N} n_{jB}} - \left(\beta_0 + \mu_0 + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}} \varepsilon^*_{ijW}}{\sum_{j=1}^{N} n_{jW}}\right) \\
&= \beta_1 + \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}} \varepsilon^*_{ijW}}{\sum_{j=1}^{N} n_{jB}} - \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}} \varepsilon^*_{ijB}}{\sum_{j=1}^{N} n_{jW}}
\end{aligned}
\tag{D.112}
$$

$$
var(\hat{\beta}_1) = var\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}} \varepsilon^*_{ijW}}{\sum_{j=1}^{N} n_{jB}} + var\frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}} \varepsilon^*_{ijB}}{\sum_{j=1}^{N} n_{jW}}
$$

As known, $var(\varepsilon_{ijB}^*)$ or $var(\varepsilon_{ijW}^*)$ are the same as $\sigma_{\varepsilon_{ijB}}^{2*}$ and $\sigma_{\varepsilon_{ijW}}^{2*}$ in different cells. I can write the above equation as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{(\sum_{j=1}^N n_{jB})\sigma_{\varepsilon_{ijB}}^{2*}}{(\sum_{j=1}^N n_{jB})^2} + \frac{(\sum_{j=1}^N n_{jW})\sigma_{\varepsilon_{ijW}}^{2*}}{(\sum_{j=1}^N n_{jW})^2} \\
var(\hat{\beta}_1) &= \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^N n_{jW}}
\end{aligned}
\tag{D.113}
$$

For condition $B_{\frac{1}{2}}$: The related sample size from (D.21) shows as $n_1 = n_2 = \cdots = n_j = n$, and $\sum_{j=1}^N n_{ijB} = \sum_{j=1}^N n_{ijW} = \frac{M}{2}$
Thus, (D.113) yields

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}} \\
var(\hat{\beta}_1) &= \frac{2(\sigma_{\varepsilon_{ijB}}^{2*} + \sigma_{\varepsilon_{ijW}}^{2*})}{M} \\
var(\beta_1) &= \frac{4\delta^2}{M}
\end{aligned}
\tag{D.114}
$$

For condition $B_{\bar{w}}$: The related sample size from (D.21) shows as

$$
\begin{aligned}
\sum_{j=1}^N n_{jB} &= \bar{w}M \\
\sum_{j=1}^N n_{jW} &= (1-\bar{w})M,
\end{aligned}
\tag{D.115}
$$

I can write (D.113) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^N n_{jW}} \\
&= \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\bar{w}M} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{(1-\bar{w})M} \\
&= \frac{(1-\bar{w})\sigma_{\varepsilon_{ijB}}^{2*} + \bar{w}\sigma_{\varepsilon_{ijW}}^{2*}}{\bar{w}(1-\bar{w})M}
\end{aligned}
\tag{D.116}
$$

For condition B_{w_j}: The related sample size from (D.20) shows as

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= n \sum_{j=1}^{N} w_j \\
\sum_{j=1}^{N} n_{jW} &= = n \sum_{j=1}^{N} (1 - w_j),
\end{aligned}
\tag{D.117}
$$

I can write (D.114) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}} \\
&= \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{n \sum_{j=1}^{N} w_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{n \sum_{j=1}^{N} (1 - w_j)} \\
&= \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{n \sum_{j=1}^{N} w_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{n(N - \sum_{j=1}^{N} w_j)} \\
&= \frac{(N - \sum_{j=1}^{N} w_j)\sigma_{\varepsilon_{ijB}}^{2*} + \sum_{j=1}^{N} w_j \sigma_{\varepsilon_{ijW}}^{2*}}{n(N - \sum_{j=1}^{N} w_j) \sum_{j=1}^{N} w_j}
\end{aligned}
\tag{D.118}
$$

For condition $U_{\frac{1}{2}}$: The related sample size from (D.20) shows as
$n_1 = n_2 = \cdots = n_j = n$, and $\sum_{j=1}^{N} n_{ijB} = \sum_{j=1}^{N} n_{ijW} = \frac{M}{2}$
Thus, (D.113) achieves

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}} \\
var(\hat{\beta}_1) &= \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}} \\
var(\hat{\beta}_1) &= \frac{4 * \frac{1}{2}(\sigma_{\varepsilon_{ijB}}^{2*} + \sigma_{\varepsilon_{ijW}}^{2*})}{4M} \\
var(\beta_1) &= \frac{4\delta^2}{M}
\end{aligned}
\tag{D.119}
$$

For condition $U_{\bar{w}}$:

The related sample size from (D.20) shows as

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= = \bar{w}M \\
\sum_{j=1}^{N} n_{jW} &= (1 - \bar{w})M
\end{aligned}
\tag{D.120}
$$

Equation (D.113) can be written as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} n_{jW}} \\
&= \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\bar{w}M} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{(1-\bar{w})M} \\
&= \frac{(1-\bar{w})\sigma^{2*}_{\varepsilon_{ijB}} + \bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{\bar{w}(1-\bar{w})M}
\end{aligned}
\tag{D.121}
$$

For condition U_{w_j}:

The related sample size from (D.20) shows as

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \sum_{j=1}^{N} w_j n_j \\
\sum_{j=1}^{N} n_{jW} &= \sum_{j=1}^{N} (1-w_j)n_j,
\end{aligned}
\tag{D.122}
$$

Equation (D.113) yields

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} n_{jW}} \\
&= \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} w_j n_j} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} (1-w_j)n_j} \\
&= \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} w_j n_j} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\left(\sum_{j=1}^{N} n_j - \sum_{j=1}^{N} w_j n_j\right)} \\
&= \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} w_j n_j} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{M - \sum_{j=1}^{N} w_j n_j} \\
&= \frac{(M - \sum_{j=1}^{N} w_j n_j)\sigma^{2*}_{\varepsilon_{ijB}} + (\sum_{j=1}^{N} w_j n_j)\sigma^{2*}_{\varepsilon_{ijW}}}{(M - \sum_{j=1}^{N} w_j n_j) \sum_{j=1}^{N} w_j n_j}
\end{aligned}
\tag{D.123}
$$

b. In RC Model

Adapting the general linearized 2-level logistic model (D.13) to the 2 level RC model, yields the following rsults: adjusted by race, and coded as 1 for black and 0 fir white race.

$$\mathbf{y}_{ij}^* = \beta_0 + x_{ij}\beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ij}^* \tag{D.124}$$

To identify the fixed effect of black race, I can rewrite the model (D.14) as the race specific models

$$
\begin{aligned}
\mathbf{y}_{ijA}^* &= \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ij}^* \quad \text{for black} \\
\mathbf{y}_{ijW}^* &= \beta_0 + \mu_{0j} + \varepsilon_{ij}^* \qquad\qquad \text{for white}
\end{aligned} \tag{D.125}
$$

Therefore, the average linearized race specific responses at j_{th} site are shown as (D.126) and (D.127) for black and white, respectively.

$$
\begin{aligned}
\bar{y}_{\cdot jB}^* &= \frac{\sum_{i=1}^{n_{jB}}\left(\beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon_{ijB}^*\right)}{n_{jB}} \qquad \text{for black} \\
&= \\
&= \frac{\sum_{i=1}^{n_{jB}}(\beta_0) + \sum_{i=1}^{n_{jB}}(\beta_1) + \sum_{i=1}^{n_{jB}}(\mu_{0j}) + \sum_{i=1}^{n_{jB}}(\mu_{1j}) + \sum_{i=1}^{n_{jB}}(\varepsilon_{ijB}^*)}{n_{jB}} \\
&= \frac{n_{jB}\beta_0 + n_{jB}\beta_1 + n_{jB}\mu_{0j} + n_{jB}\mu_{1j} + \sum_{i=1}^{n_{jB}}(\varepsilon_{ijB}^*)}{n_{jB}} \\
&= \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \bar{\varepsilon}_{\cdot jB}^* \qquad (E\varepsilon_{\cdot jB}^* = 0) \\
&= \beta_0 + \beta_1 + \mu_{0j} + \mu_{1j}
\end{aligned} \tag{D.126}
$$

$$
\begin{aligned}
\bar{y}_{\cdot jw}^* &= \frac{\sum_{i=1}^{n_{jW}}\left(\beta_0 + \mu_{0j} + \varepsilon_{ijW}^*\right)}{\sum_{i=1}^{n_{jW}} 1} \qquad\qquad \text{for white} \\
&= \frac{\sum_{i=1}^{n_{jW}}(\beta_0) + \sum_{i=1}^{n_{jW}}(\mu_{0j}) + \sum_{i=1}^{n_{jW}}(\varepsilon_{ijW}^*)}{n_{jW}} \\
&= \frac{n_{jW}\beta_0 + n_{jW}\mu_{0j} + \sum_{i=1}^{n_{jW}}(\varepsilon_{ijW}^*)}{n_{jW}} \\
&= \beta_0 + \mu_{0j} + \bar{\varepsilon}_{\cdot jW}^* \qquad (E\varepsilon_{\cdot jW}^* = 0) \\
&= \beta_0 + \mu_{0j}
\end{aligned} \tag{D.127}
$$

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Similarly, the average outcome yields

$$
\begin{aligned}
\bar{y}^*_{..B} &= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon^*_{ijB})}{\sum_{j=1}^{N} n_{jB}} && \text{for black} \\
&= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\beta_0) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\beta_1) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\mu_{0j}) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\mu_{1j}) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jB}}(\varepsilon^*_{ijB})}{n_B} \\
&= \frac{n_B\beta_0 + n_B\beta_1 + \sum_{j=1}^{N} n_{jB}\mu_{0j} + \sum_{j=1}^{N} n_{jB}\mu_{1j} + \sum_{i=1}^{n_{jB}}\sum_{j=1}^{N}(\varepsilon^*_{ijB})}{n_B} \\
&= \beta_0 + \beta_1 + \frac{\sum_{j=1}^{N} n_{jB}\mu_{0j}}{n_B} + \frac{\sum_{j=1}^{N} n_{jB}\mu_{1j}}{n_B} + \bar{\varepsilon}^*_{..B} \\
&= \beta_0 + \beta_1 + \bar{\mu}_{0B} + \bar{\mu}_{1B} + \bar{\varepsilon}^*_{..B} && (E\mu_0 = 0 \quad \& \quad E\mu_1 = 0) \\
&= \beta_0 + \beta_1 && \text{(D.128)}
\end{aligned}
$$

$$
\begin{aligned}
\bar{y}^*_{..W} &= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\beta_0 + \mu_{0j} + \varepsilon^*_{ijW})}{\sum_{j=1}^{N} n_{jW}} && \text{for white} \\
&= \frac{\sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\beta_0) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\mu_{0j}) + \sum_{j=1}^{N}\sum_{i=1}^{n_{jW}}(\varepsilon^*_{ijW})}{n_W} \\
&= \frac{n_W\beta_0 + \sum_{j=1}^{N} n_{jW}\mu_{0j} + \sum_{i=1}^{n_{jW}}\sum_{j=1}^{N}(\varepsilon^*_{ijW})}{n_W} \\
&= \beta_0 + \frac{\sum_{j=1}^{N} n_{jW}\mu_{0j}}{n_W} + \bar{\varepsilon}^*_{..W} \\
&= \beta_0 + \bar{\mu}_{0W} + \bar{\varepsilon}^*_{..W} && (E\mu_0 = 0 \quad \& \quad E\mu_1 = 0) \\
&= \beta_0 && \text{(D.129)}
\end{aligned}
$$

Therefore, the GLS estimate of race can be obtained by

$$
\bar{y}^*_{..B} - \bar{y}^*_{..W} = \beta_0 + \beta_1 - \beta_0 = \beta_1 \tag{D.130}
$$

By applying corresponding f(H) to (D.12) and (D.11), the modified $\mathbf{y}^*_{ij}$ and ε^*_{ij} result in

$$
\begin{aligned}
\mathbf{y}^*_{ij} &= (\mathbf{y}_{ij} - \tilde{\pi}_{ij})[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} + \beta_0 + x_{ij}\beta_1 \\
\varepsilon^*_{ij} &= \varepsilon_{ij}[\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} \tag{D.131}
\end{aligned}
$$

Then, applying $V_j = \sigma^2_{\mu_0}$ to $\mathbf{var}(\mathbf{Y}^*_{ij})$ as (D.17) for the RI model yields

$$
\mathbf{var}(\mathbf{Y}^*_{ij}) = \sigma^2_{\mu_0} + \sigma^2_{\mu_1} + [\tilde{\pi}_{ij}(1 - \tilde{\pi}_{ij})]^{-1} \tag{D.132}
$$

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Based on the linearized 2-level logistic model (D.13) and by applying the GLS estimate of β_1 as (D.130), I get

$$
\begin{aligned}
\hat{\beta}_1 &= \bar{y}^*_{..B} - \bar{y}^*_{..W} \\
\hat{\beta}_1 &= \frac{\sum_{j=1}^{N} \bar{y}^*_{.jB} - \sum_{j=1}^{N} \bar{y}^*_{.jW}}{N} \\
\hat{\beta}_1 &= \frac{\sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} y^*_{ijB}}{n_{jB}} - \sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jW}} y^*_{ijW}}{n_{jW}}}{N}
\end{aligned}
\tag{D.133}
$$

I have presented y_{ijB} and y_{ijW} as (D.125). Plugging in (D.133), I will get

$$
\hat{\beta}_1 = \frac{\sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} \{\beta_0 + \beta_1 + \mu_{0j} + \mu_{1j} + \varepsilon^*_{ij}\}}{n_{jB}} - \sum_{j=1}^{N} \frac{\sum_{i=1}^{n_{jB}} \{\beta_0 + \mu_{0j} + \varepsilon^*_{ij}\}}{n_{jW}}}{N}
$$

β_0 and β_1 will be constant everywhere. μ_{0j} will be constant at j_{th} hospital.

$$
\begin{aligned}
\hat{\beta}_1 &= \beta_0 + \beta_1 + \frac{\sum_{j=1}^{N} \mu_{0j}}{N} + \frac{\sum_{j=1}^{N} \mu_{1j}}{N} + \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} \varepsilon^*_{ijB}}{\sum_{j=1}^{N} n_{jB}} - (\beta_0 + \frac{\sum_{j=1}^{N} \mu_{0j}}{N} + \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} \varepsilon^*_{ijW}}{\sum_{j=1}^{N} n_{jW}}) \\
&= \beta_1 + \frac{\sum_{j=1}^{N} \mu_{1j}}{N} + \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} \varepsilon^*_{ijB}}{\sum_{j=1}^{N} n_{jB}} - \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jW}} \varepsilon^*_{ijW}}{\sum_{j=1}^{N} n_{jW}}
\end{aligned}
\tag{D.134}
$$

$$
var(\hat{\beta}_1) = var(\beta_1) + var(\frac{\sum_{j=1}^{N} \mu_{1j}}{N}) + var\frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} \varepsilon^*_{ijW}}{\sum_{j=1}^{N} n_{jW}} + var\frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} \varepsilon^*_{ijB}}{\sum_{j=1}^{N} n_{jB}}
$$

As known, $var(\varepsilon^*_{ijB})$ or $var(\varepsilon^*_{ijW})$ are the same as $\sigma^{2*}_{\varepsilon_{ijB}}$ and $\sigma^{2*}_{\varepsilon_{ijW}}$ in different cell. At the same time, $var(\mu_{1j}) = \sigma^2_{\mu_1}$ at any hospital. I can write the above equation as

$$
\begin{aligned}
var(\hat{\beta}_1) &= var(\beta_1) + \frac{\sum_{j=1}^{N} var(\mu_{1j})}{N^2}) + \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} var\varepsilon^*_{ijW}}{n_W^2} + \frac{\sum_{j=1}^{N} \sum_{i=1}^{n_{jB}} var\varepsilon^*_{ijB}}{n_W^2} \\
&= \frac{N\sigma^2_{\mu_1}}{N^2} + \frac{(\sum_{j=1}^{N} n_{jB})\sigma^{2*}_{\varepsilon_{ijB}}}{(\sum_{j=1}^{N} n_{jB})^2} + \frac{(\sum_{j=1}^{N} n_{jW})\sigma^{2*}_{\varepsilon_{ijW}}}{(\sum_{j=1}^{N} n_{jW})^2} \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{n_B \sigma^{2*}_{\varepsilon_{ijB}}}{n_B^2} + \frac{n_W \sigma^{2*}_{\varepsilon_{ijW}}}{n_W^2} \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{n_B} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{n_W}
\end{aligned}
$$

For condition $B_{\frac{1}{2}}$: The related sample size from (D.21) shows as $n_1 = n_2 = \cdots = n_j = n$, and $\sum_{j=1}^{N} n_{ijB} = \sum_{j=1}^{N} n_{ijW} = \frac{M}{2}$

Thus, (D.135) yields

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma^2_{\mu_1}}{N} + \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\frac{M}{2}} + \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\frac{M}{2}} \\
var(\hat{\beta}_1) &= \frac{\sigma^2_{\mu_1}}{N} + \frac{2(\sigma^{2*}_{\varepsilon_{ijB}} + \sigma^{2*}_{\varepsilon_{ijW}})}{M} \\
var(\beta_1) &= \frac{\sigma^2_{\mu_1} n + 4\delta^2}{M}
\end{aligned} \tag{D.136}
$$

For condition $B_{\bar{w}}$: The related sample size from (D.20) shows as

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= \bar{w}M \\
\sum_{j=1}^{N} n_{jW} &= (1 - \bar{w})M,
\end{aligned} \tag{D.137}
$$

I can write (D.136) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma^2_{\mu_1}}{N} + \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{\sum_{j=1}^{N} n_{jW}} \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{\sigma^{2*}_{\varepsilon_{ijB}}}{\bar{w}M} + \frac{\sigma^{2*}_{\varepsilon_{ijW}}}{(1 - \bar{w})M} \\
&= \frac{\sigma^2_{\mu_1}}{N} + \frac{(1 - \bar{w})\sigma^{2*}_{\varepsilon_{ijB}} + \bar{w}\sigma^{2*}_{\varepsilon_{ijW}}}{\bar{w}(1 - \bar{w})M}
\end{aligned} \tag{D.138}
$$

For condition B_{w_j}: The related sample size from (D.20) shows as

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= n \sum_{j=1}^{N} w_j \\
\sum_{j=1}^{N} n_{jW} &= = n \sum_{j=1}^{N} (1 - w_j),
\end{aligned} \tag{D.139}
$$

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I can write (D.136) as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{n \sum_{j=1}^{N} w_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{n \sum_{j=1}^{N} (1 - w_j)} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{n \sum_{j=1}^{N} w_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{n (N - \sum_{j=1}^{N} w_j)} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{(N - \sum_{j=1}^{N} w_j) \sigma_{\varepsilon_{ijB}}^{2*} + \sum_{j=1}^{N} w_j \sigma_{\varepsilon_{ijW}}^{2*}}{n (N - \sum_{j=1}^{N} w_j) \sum_{j=1}^{N} w_j}
\end{aligned}
\tag{D.140}
$$

For condition $U_{\frac{1}{2}}$: The related sample size from (D.20) shows as
$n_1 = n_2 = \cdots = n_j = n$, and $\sum_{j=1}^{N} n_{ijB} = \sum_{j=1}^{N} n_{ijW} = \frac{M}{2}$
Thus, (D.136) achieves

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^{N} n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^{N} n_{jW}} \\
var(\hat{\beta}_1) &= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\frac{M}{2}} \\
var(\hat{\beta}_1) &= \frac{\sigma_{\mu_1}^2}{N} + \frac{2(\sigma_{\varepsilon_{ijB}}^{2*} + \sigma_{\varepsilon_{ijW}}^{2*})}{M} \\
var(\beta_1) &= \frac{4\delta^2}{M}
\end{aligned}
\tag{D.141}
$$

For condition $U_{\bar{w}}$:

The related sample size from (D.20) shows as

$$
\begin{aligned}
\sum_{j=1}^{N} n_{jB} &= = \bar{w}M \\
\sum_{j=1}^{N} n_{jW} &= (1 - \bar{w})M
\end{aligned}
\tag{D.142}
$$

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Equation (D.136) can be written as

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^N n_{jW}} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\bar{w}M} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{(1-\bar{w})M} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{(1-\bar{w})\sigma_{\varepsilon_{ijB}}^{2*} + \bar{w}\sigma_{\varepsilon_{ijW}}^{2*}}{\bar{w}(1-\bar{w})M}
\end{aligned}
\tag{D.143}
$$

For condition U_{w_j}:

The related sample size from (D.20) shows as

$$
\begin{aligned}
\sum_{j=1}^N n_{jB} &= \sum_{j=1}^N w_j n_j \\
\sum_{j=1}^N n_{jW} &= \sum_{j=1}^N (1-w_j)n_j,
\end{aligned}
\tag{D.144}
$$

Equation (D.136) yields

$$
\begin{aligned}
var(\hat{\beta}_1) &= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N n_{jB}} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^N n_{jW}} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N w_j n_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\sum_{j=1}^N (1-w_j)n_j} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N w_j n_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{\left(\sum_{j=1}^N n_j - \sum_{j=1}^N w_j n_j\right)} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{\sigma_{\varepsilon_{ijB}}^{2*}}{\sum_{j=1}^N w_j n_j} + \frac{\sigma_{\varepsilon_{ijW}}^{2*}}{M - \sum_{j=1}^N w_j n_j} \\
&= \frac{\sigma_{\mu_1}^2}{N} + \frac{(M - \sum_{j=1}^N w_j n_j)\sigma_{\varepsilon_{ijB}}^{2*} + (\sum_{j=1}^N w_j n_j)\sigma_{\varepsilon_{ijW}}^{2*}}{(M - \sum_{j=1}^N w_j n_j)\sum_{j=1}^N w_j n_j}
\end{aligned}
\tag{D.145}
$$

APPENDIX E

IMAGE OF MLWIN RESULTS USING MLWIN VERSION 2.02

$$\text{anysoc30}_{ij} \sim \text{Binomial}(\text{denom}_{ij}, \pi_{ij})$$
$$\text{logit}(\pi_{ij}) = \beta_{0j}\text{cons} + \text{-0.113(0.047)Black}_{ij}$$
$$\beta_{0j} = \text{-2.517(0.031)} + u_{0j}$$

$$\begin{bmatrix} u_{0j} \end{bmatrix} \sim N(0, \Omega_u) : \Omega_u = \begin{bmatrix} 0.048(0.013) \end{bmatrix}$$

$$\text{var}(\text{anysoc30}_{ij}|\pi_{ij}) = \pi_{ij}(1 - \pi_{ij})/\text{denom}_{ij}$$

Figure E1: RI Model for Pneumonia Patient Younger than 65, Using RIGLS PQL2

	# 1
fixed : cons	1.000
fixed : black	0.000
constant(k)	0.000
function result(f)	-2.517
f-k	-2.517
chi sq, (f-k)=0. (1df)	6608.021
+/- 95% sep.	0.061
+/- 95% joint	0.061

joint chi sq test(1df) = 6608.021

○ random ⊙ fixed # of functions 1   [Calc] [Help]

	# 1
site : cons/cons	1.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.048
f-k	0.048
chi sq, (f-k)=0. (1df)	13.674
+/- 95% sep.	0.025
+/- 95% joint	0.025

joint chi sq test(1df) = 13.674

⊙ random ○ fixed # of functions 1   [Calc] [Help]

(a) Fixed Effect   (b) Random Effect

Figure E2: Hypothesis Test for Intercept Term in the RI Model, Using RIGLS PQL2

Figure E3: Hypothesis Test for Black as Fixed Effect in the RI Model, Using RIGLS PQL2

Figure E4: RC Model for Pneumonia Patients Younger Than 65, Using RIGLS PQL2

	#1
fixed : cons	1.000
fixed : black	0.000
constant(k)	0.000
function result(f)	-2.509
f-k	-2.509
chi sq, (f-k)=0. (1df)	296.906
+/- 95% sep.	0.058
+/- 95% joint	0.058

joint chi sq test(1df) = 7296.906

○ random ⦿ fixed # of functions 1   Calc Help

	#1
site : cons/cons	1.000
site : black/cons	0.000
site : black/black	0.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.036
f-k	0.036
chi sq, (f-k)=0. (1df)	7.282
+/- 95% sep.	0.026
+/- 95% joint	0.026

joint chi sq test(1df) = 7.282

⦿ random ○ fixed # of functions 1   Calc Help

(a) Fixed Effect   (b) Random Effect

Figure E5: Hypothesis Test for Intercept Term in the RC Model, Using RIGLS PQL2

	#1
fixed : cons	0.000
fixed : black	1.000
constant(k)	0.000
function result(f)	-0.155
f-k	-0.155
chi sq, (f-k)=0. (1df)	6.649
+/- 95% sep.	0.118
+/- 95% joint	0.118

joint chi sq test(1df) = 6.649

○ random ⦿ fixed # of functions 1   Calc Help

	#1
site : cons/cons	0.000
site : black/cons	0.000
site : black/black	1.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.094
f-k	0.094
chi sq, (f-k)=0. (1df)	4.078
+/- 95% sep.	0.091
+/- 95% joint	0.091

joint chi sq test(1df) = 4.078

⦿ random ○ fixed # of functions 1   Calc Help

(a) Fixed Effect   (b) Random Effect

Figure E6: Hypothesis Test for Black in the RC Model, Using RIGLS PQL2

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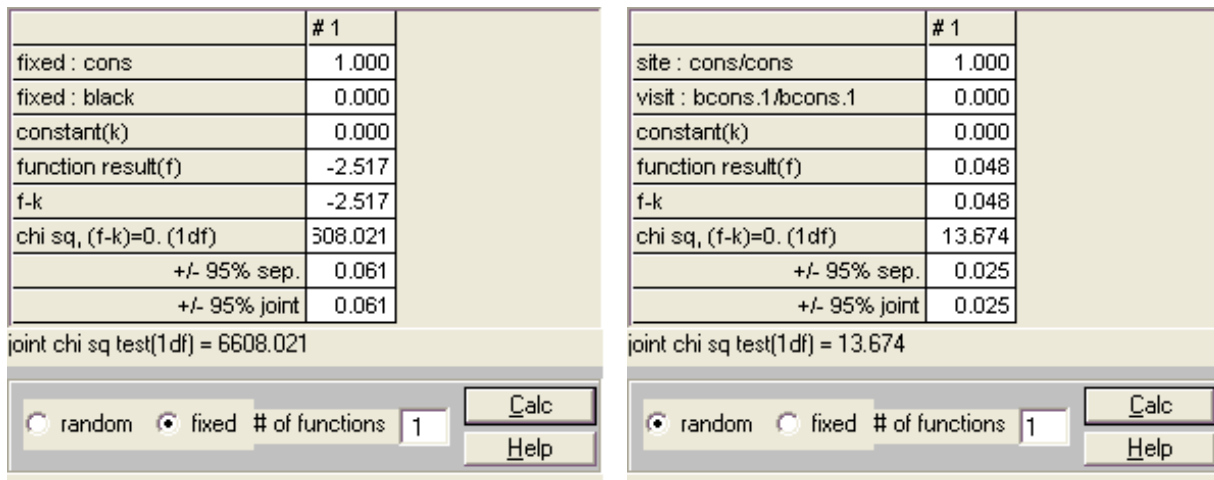$$\text{anysoc30}_{ij} \sim \text{Binomial}(\text{denom}_{ij}, \pi_{ij})$$

$$\text{logit}(\pi_{ij}) = \beta_{0j}\text{cons} + \text{-0.134(0.059)Black}_{ij}$$

$$\beta_{0j} = \text{-2.439(0.057)} + u_{0j}$$

$$\begin{bmatrix} u_{0j} \end{bmatrix} \sim \text{N}(0, \ \Omega_u) \ : \ \Omega_u = \begin{bmatrix} 0.069(0.023) \end{bmatrix}$$

$$\text{var}(\text{anysoc30}_{ij}|\pi_{ij}) = \pi_{ij}(1 - \pi_{ij})/\text{denom}_{ij}$$

Figure E7: RI Model for Pneumonia Patient Younger Than 65 in Q2Q4, Using RIGLS PQL2

	# 1
fixed : cons	1.000
fixed : black	0.000
constant(k)	0.000
function result(f)	-2.415
f-k	-2.415
chi sq, (f-k)=0. (1df)	439.985
+/- 95% sep.	0.096
+/- 95% joint	0.096

joint chi sq test(1df) = 2439.985

random   • fixed   # of functions   1   Calc   Help

	# 1
site : cons/cons	1.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.069
f-k	0.069
chi sq, (f-k)=0. (1df)	8.963
+/- 95% sep.	0.045
+/- 95% joint	0.045

joint chi sq test(1df) = 8.963

• random   fixed   # of functions   1   Calc   Help

(a) Fixed Effect   (b) Random Effect

Figure E8: Hypothesis Test for Intercept Term in the RI Model in Q2Q4, Using RIGLS PQL2

Figure E9: Hypothesis Test for Black as Fixed Effect in the RI Model in Q2Q4, Using RIGLS PQL2

$$\text{anysoc30}_{ij} \sim \text{Binomial}(\text{denom}_{ij}, \pi_{ij})$$
$$\text{logit}(\pi_{ij}) = \beta_{0j}\text{cons} + \beta_{1j}\text{Black}_{ij}$$
$$\beta_{0j} = -2.415(0.049) + u_{0j}$$
$$\beta_{1j} = -0.191(0.081) + u_{1j}$$

$$\begin{bmatrix} u_{0j} \\ u_{1j} \end{bmatrix} \sim N(0, \ \Omega_u) \ : \ \Omega_u = \begin{bmatrix} 0.036(0.020) \\ 0.005(0.026) \ \ 0.116(0.058) \end{bmatrix}$$

$$\text{var}(\text{anysoc30}_{ij}|\pi_{ij}) = \pi_{ij}(1 - \pi_{ij})/\text{denom}_{ij}$$

Figure E10: RC Model for Pneumonia patients younger than 65 in Q2Q4, Using RIGLS PQL2

	#1
fixed : cons	1.000
fixed : black	0.000
constant(k)	0.000
function result(f)	-2.415
f-k	-2.415
chi sq, (f-k)=0. (1df)	439.985
+/- 95% sep.	0.096
+/- 95% joint	0.096

joint chi sq test(1df) = 2439.985

	#1
site : cons/cons	1.000
site : black/cons	0.000
site : black/black	0.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.036
f-k	0.036
chi sq, (f-k)=0. (1df)	3.172
+/- 95% sep.	0.040

joint chi sq test(1df) = 3.172

   (a) Fixed Effect   (b) Random Effect

Figure E11: Hypothesis Test for Intercept Term in RC Model in Q2Q4, Using RIGLS PQL2

	#1
fixed : cons	0.000
fixed : black	1.000
constant(k)	0.000
function result(f)	-0.191
f-k	-0.191
chi sq, (f-k)=0. (1df)	5.589
+/- 95% sep.	0.158
+/- 95% joint	0.158

joint chi sq test(1df) = 5.589

	#1
fixed : cons	0.000
fixed : black	1.000
constant(k)	0.000
function result(f)	-0.191
f-k	-0.191
chi sq, (f-k)=0. (1df)	5.589
+/- 95% sep.	0.158
+/- 95% joint	0.158

joint chi sq test(1df) = 5.589

   (a) Fixed Effect   (b) Random Effect

Figure E12: Hypothesis Test for Black in RC Model in Q2Q4, Using RIGLS PQL2

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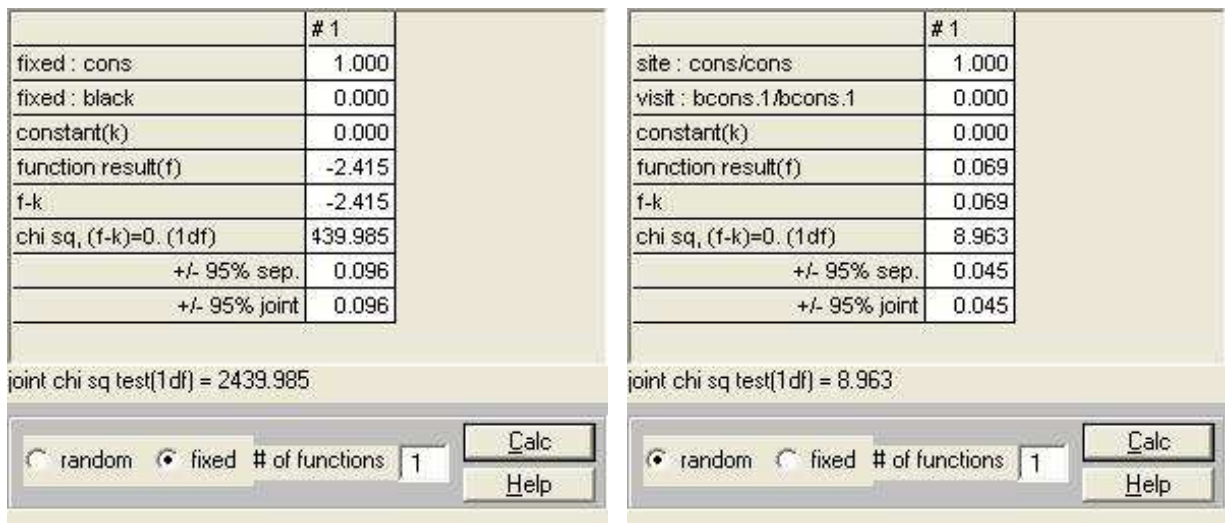$$\text{anysoc30}_{ij} \sim \text{Binomial}(\text{denom}_{ij}, \pi_{ij})$$
$$\text{logit}(\pi_{ij}) = \beta_{0j}\text{cons} + \text{-0.134(0.059)}\text{Black}_{ij}$$
$$\beta_{0j} = \text{-2.439(0.057)} + u_{0j}$$

$$\begin{bmatrix} u_{0j} \end{bmatrix} \sim N(0,\ \Omega_u) : \Omega_u = \begin{bmatrix} 0.069(0.023) \end{bmatrix}$$

$$\text{var}(\text{anysoc30}_{ij}|\pi_{ij}) = \pi_{ij}(1 - \pi_{ij})/\text{denom}_{ij}$$

Figure E13: RI Model for Pneumonia Patients Younger Than 65, Using IGLS MQL1

	# 1
fixed : cons	1.000
fixed : black	0.000
constant(k)	0.000
function result(f)	-2.517
f-k	-2.517
chi sq, (f-k)=0. (1df)	608.021
+/- 95% sep.	0.061
+/- 95% joint	0.061
joint chi sq test(1df) = 6608.021	

○ random ⊙ fixed # of functions 1   Calc   Help

	# 1
site : cons/cons	1.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.048
f-k	0.048
chi sq, (f-k)=0. (1df)	13.674
+/- 95% sep.	0.025
+/- 95% joint	0.025
joint chi sq test(1df) = 13.674	

⊙ random ○ fixed # of functions 1   Calc   Help

(a) Fixed Effect

(b) Random Effect

Figure E14: Hypothesis Test for Intercept Term in the RI Model, Using IGLS MQL1

	# 1
fixed : cons	0.000
fixed : black	1.000
constant(k)	0.000
function result(f)	-0.113
f-k	-0.113
chi sq, (f-k)=0. (1df)	5.669
+/- 95% sep.	0.093
+/- 95% joint	0.093

joint chi sq test(1df) = 5.669

○ random ⊙ fixed # of functions [1]

Calc

Help

Figure E15: Hypothesis Test for Black as Fixed Effect in the RI Model, Using IGLS MQL1

$\text{anysoc30}_{ij} \sim \text{Binomial}(\text{denom}_{ij}, \pi_{ij})$

$\text{logit}(\pi_{ij}) = \beta_{0j}\text{cons} + \beta_{1j}\text{Black}_{ij}$

$\beta_{0j} = \text{-2.415}(0.049) + u_{0j}$

$\beta_{1j} = \text{-0.191}(0.081) + u_{1j}$

$$\begin{bmatrix} u_{0j} \\ u_{1j} \end{bmatrix} \sim N(0, \ \Omega_u) \ : \ \Omega_u = \begin{bmatrix} 0.036(0.020) & \\ 0.005(0.026) & 0.116(0.058) \end{bmatrix}$$

$\text{var}(\text{anysoc30}_{ij}|\pi_{ij}) = \pi_{ij}(1 - \pi_{ij})/\text{denom}_{ij}$

Figure E16: RC Model for Pneumonia Patient Younger than 65, Using IGLS MQL1

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	# 1
fixed : cons	1.000
fixed : black	0.000
constant(k)	0.000
function result(f)	-2.509
f-k	-2.509
chi sq, (f-k)=0. (1df)	296.906
+/- 95% sep.	0.058
+/- 95% joint	0.058

joint chi sq test(1df) = 7296.906

○ random ◉ fixed # of functions 1   [Calc] [Help]

	# 1
site : cons/cons	1.000
site : black/cons	0.000
site : black/black	0.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.036
f-k	0.036
chi sq, (f-k)=0. (1df)	7.282
+/- 95% sep.	0.026
+/- 95% joint	0.026

joint chi sq test(1df) = 7.282

◉ random ○ fixed # of functions 1   [Calc] [Help]

(a) Fixed Effect   (b) Random Effect

Figure E17: Hypothesis Test for Intercept Term in the RC Model, Using IGLS MQL1

	# 1
fixed : cons	0.000
fixed : black	1.000
constant(k)	0.000
function result(f)	-0.155
f-k	-0.155
chi sq, (f-k)=0. (1df)	6.649
+/- 95% sep.	0.118
+/- 95% joint	0.118

joint chi sq test(1df) = 6.649

○ random ◉ fixed # of functions 1   [Calc] [Help]

	# 1
site : cons/cons	0.000
site : black/cons	0.000
site : black/black	1.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.094
f-k	0.094
chi sq, (f-k)=0. (1df)	4.078
+/- 95% sep.	0.091
+/- 95% joint	0.091

joint chi sq test(1df) = 4.078

◉ random ○ fixed # of functions 1   [Calc] [Help]

(a) Fixed Effect   (b) Random Effect

Figure E18: Hypothesis Test for Black in the RC Model, Using IGLS MQL1

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$$\text{anysoc30}_{ij} \sim \text{Binomial}(\text{denom}_{ij},\ \pi_{ij})$$
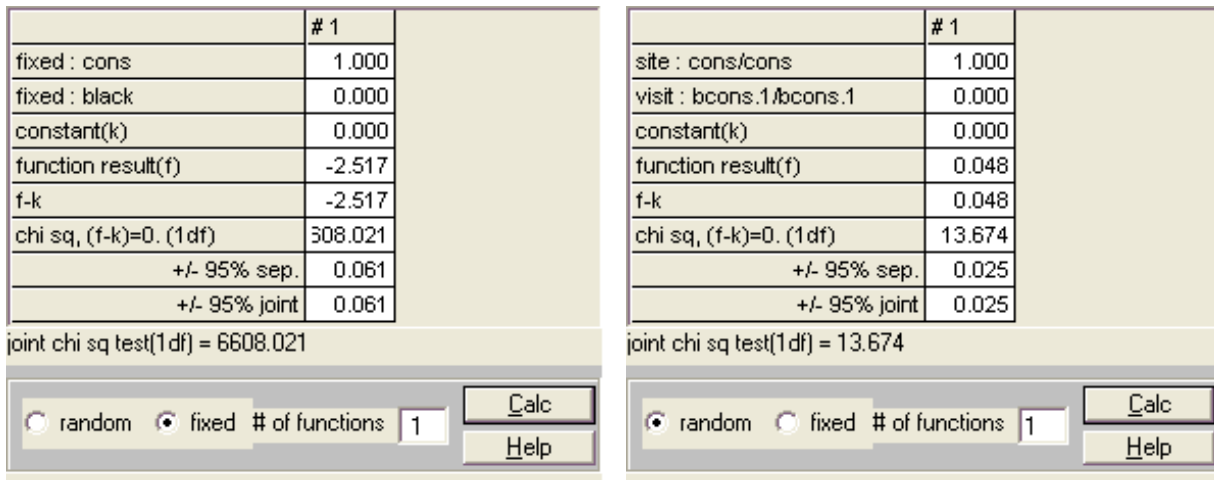
$$\text{logit}(\pi_{ij}) = \beta_{0j}\text{cons} + \textcolor{green}{-0.131(0.059)}\text{Black}_{ij}$$

$$\beta_{0j} = \textcolor{green}{-2.412(0.056)} + u_{0j}$$

$$\begin{bmatrix} u_{0j} \end{bmatrix} \sim \text{N}(0,\ \Omega_u)\ :\ \Omega_u = \begin{bmatrix} \textcolor{green}{0.069(0.023)} \end{bmatrix}$$

$$\text{var}(\text{anysoc30}_{ij}|\pi_{ij}) = \pi_{ij}(1 - \pi_{ij})/\text{denom}_{ij}$$

Figure E19: RI Model for Pneumonia Patients Younger Than 65 in Q2 to Q4, Using IGLS MQL1

	# 1
fixed : cons	1.000
fixed : black	0.000
constant(k)	0.000
function result(f)	-2.400
f-k	-2.400
chi sq, (f-k)=0. (1df)	442.043
+/- 95% sep.	0.095
+/- 95% joint	0.095

joint chi sq test(1df) = 2442.043

○ random ⦿ fixed # of functions 1   Calc   Help

(a) Fixed Effect

	# 1
site : cons/cons	1.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.069
f-k	0.069
chi sq, (f-k)=0. (1df)	9.207
+/- 95% sep.	0.044
+/- 95% joint	0.044

joint chi sq test(1df) = 9.207

⦿ random ○ fixed # of functions 1   Calc   Help
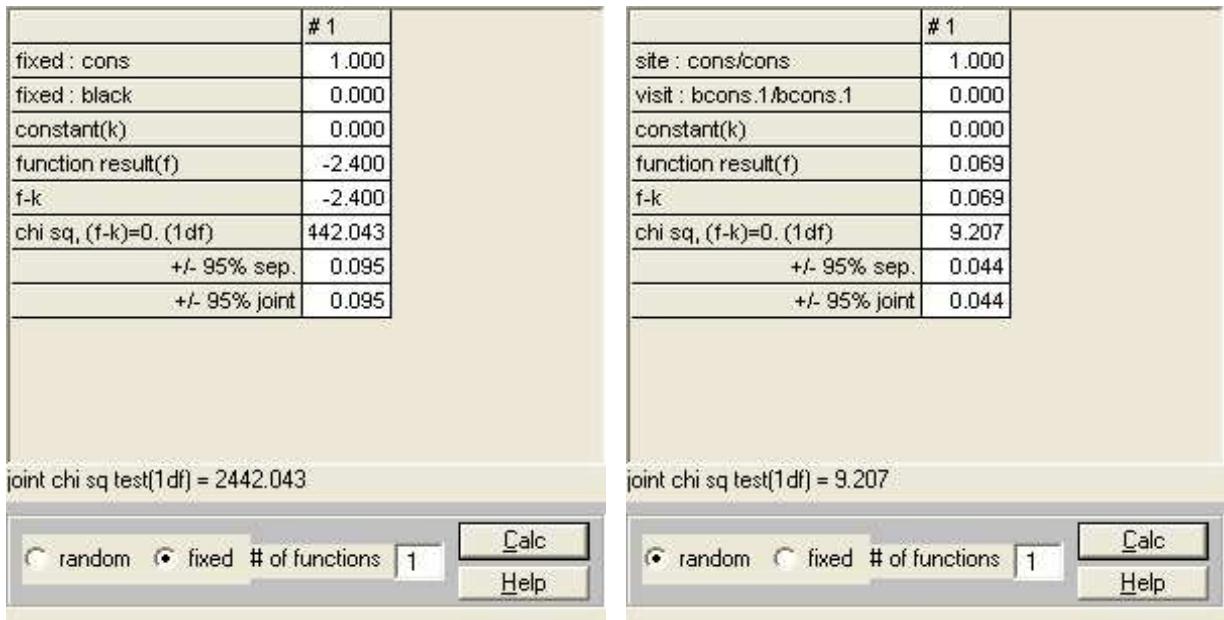
(b) Random Effect

Figure E20: Hypothesis Test for Intercept Term in RI Model in Q2 to Q4, using IGLS MQL1

Figure E21: Hypothesis Test for Black as Fixed Effect in the RI Model in Q2 to Q4, Using IGLS MQL1

Figure E22: RC Model for Pneumonia Patient Younger than 65 in Q2 to Q4, Using IGLS MQL1

	# 1
fixed : cons	1.000
fixed : black	0.000
constant(k)	0.000
function result(f)	-2.400
f-k	-2.400
chi sq, (f-k)=0. (1df)	442.043
+/- 95% sep.	0.095
+/- 95% joint	0.095

joint chi sq test(1df) = 2442.043

○ random ⊙ fixed # of functions 1   Calc   Help

(a) Fixed Effect

	# 1
site : cons/cons	1.000
site : black/cons	0.000
site : black/black	0.000
visit : bcons.1/bcons.1	0.000
constant(k)	0.000
function result(f)	0.036
f-k	0.036
chi sq, (f-k)=0. (1df)	3.092
+/- 95% sep.	0.040
+/- 95% joint	0.040

joint chi sq test(1df) = 3.092

⊙ random ○ fixed # of functions 1   Calc   Help

(b) Random Effect

Figure E23: Hypothesis Test for Intercept Term in RC Model in Q2 to Q4, Using IGLS MQL1

	# 1
fixed : cons	0.000
fixed : black	1.000
constant(k)	0.000
function result(f)	-0.137
f-k	-0.137
chi sq, (f-k)=0. (1df)	2.870
+/- 95% sep.	0.159
+/- 95% joint	0.159

joint chi sq test(1df) = 2.870

○ random ● fixed # of functions 1   Calc   Help

(a) Fixed Effect

	# 1
fixed : cons	0.000
fixed : black	1.000
constant(k)	0.000
function result(f)	-0.137
f-k	-0.137
chi sq, (f-k)=0. (1df)	2.870
+/- 95% sep.	0.159
+/- 95% joint	0.159

joint chi sq test(1df) = 2.870

○ random ● fixed # of functions 1   Calc   Help

(b) Random Effect

Figure E24: Hypothesis Test for Black in RC Model in Q2 to Q4, Using IGLS MQL1

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APPENDIX F

PROGRAM FOR SIMULATION STUDY

A. MACRO FUNCTION TO TRANSFER STATA TO MLWIN

Stata macro Stata2Mlwin can be downloaded from below web site:

http://www.ats.ucla.edu/stat/mlwin/faq/stata2mlwin.htm.

This function is written for a continuous outcome. An optimized macro in the same name is developed for binary outcome data. This ado file is stored in "C:\ado\plus\s". I attached this program in the next few pages. I modified this macro for fitting 2-level logistic model fitting.

After I submit the following codes in Stata stata2mlwin "C:\data\pnaless65", a MLwiN obey file is created and stored as "C:\data\pnaless65.obe".

In MLwin's macro window, we can submit below macro to transfer and save pnaless.ws.

obey "C:\data\pnaless65.obe"

save "C:\data\pnaless65.ws"

Macro function to transfer Stata to MLwin

```
*! Version 1.0
*! Version 1.1, converts string vars to numeric via "encode"
*! Version 1.2, adds missing() option, with -12345 as default missing code
*!              Handles version 8 missing codes .a etc.
*! Version 1.2.1 Added message about sorting data
*! Add need variable for 2-level logistic model
capture program drop stata2mlwin
program define stata2mlwin
  version 7
  syntax using/ , [ replace clear nocons missing(integer -12345 ) ]

  use "`using'" , `clear'
  if "`nobcons'" == "" {
    capture local hascons : type bcons
    if _rc != 0 {
      gen bcons = 1
      order bcons
    }
    else {
      display as error "Variable bcons already exists, no binary constant created"
      display "Conversion continues"
    }
  }

  if "`nodenom'" == "" {
    capture local hascons : type denom
    if _rc != 0 {
      gen denom= 1
      order denom
    }
    else {
      display as error "Variable denom already exists, no denom created"
      display "Conversion continues"
    }
  }


  if "`nocons'" == "" {
    capture local hascons : type cons
    if _rc != 0 {
      gen cons = 1
      order cons
    }
```

```
  else {
    display as error "Variable cons already exists, no constant created"
    display "Conversion continues"
  }
}


tempvar out
capture file close `out'

quietly file open `out' using "`using'.obe", write text `replace'

unab varlist : *
local varcnt: word count `varlist'
* display " varlist is `varlist' has `varcnt'"

foreach var of local varlist {
  local vartype : type `var'
  if (substr("`vartype'",1,3)=="str") {
    display "encoding `var'"
    tempvar tempenc
    encode `var', generate(`tempenc')
    drop `var'
    rename `tempenc' `var'
  }
}


display "Missing values stored as `missing'
display "(You can change this with the missing() option.)"
display "In MLwiN, choose Options Worksheet then Numbers"
display "to tell it that values that are `missing' are missing."

quietly count
local ncases = `r(N)'

* file write `out' "wipe" _newline
file write `out' "echo 0" _newline
file write `out' "assign c1-c`varcnt'" _newline

local i = 1
while (`i' <= `ncases') {
  if mod(`i' , 100 ) == 0 {
    display _column(1) "." _continue
  }
  foreach var of local varlist {
```

```
     local vartype : type `var'
     if (("`vartype'"=="byte") | ("`vartype'"=="int") | ("`vartype'"== "long") |
("`vartype'"== "float") | ("`vartype'"== "double")) {
        if (`var'[`i'] >= .) {
           file write `out' "`missing'" " "
        }
        else {
           file write `out' (`var'[`i']) " "
        }
     }
     else {
        file write `out' (`var'[`i']) " "
     }
   }
   file write `out' _newline
   local i = `i' + 1
}
display

file write `out' "finish" _newline
file write `out' "echo 1" _newline

file write `out' _newline
local i = 0
foreach var of local varlist {
   local i = `i' + 1
   file write `out' "name c`i' '`var''" _newline
}

file write `out' _newline
local i = 0
foreach var of local varlist {
   local i = `i' + 1
   makelab `var' `i' `ncases' `out'
}

local pwd : pwd
* if index("`using'","\") == 0 {
*   file write `out'  _newline "save `pwd'" "\" "`using'.ws" _newline
* }
* else {
*   file write `out'  _newline "save `using'.ws" _newline
* }
```

```
      file close `out'


      display as text "Looks like this was a success."
      display as text "To convert the file to MLwiN, start MLwiN and then"
      display as text "Choose 'Data Manipulation -> Command Interface"
      display as text "then at the command prompt type"
      display as input "  wipe"
      display as text "which clears out any data (if any), then type"
      if index("`using'","\") == 0 {
        display as input "  obey `pwd'" "\" "`using'.obe"
      }
      else {
        display as input "  obey `using'.obe"
      }
      display as text "which runs the program to make the MLwiN data file."
      display as text "You can then choose 'File' -> 'Save as' to save the file."

      display
      display "NOTE: Please be sure your data is sorted based on the levels"
      display "of your model.  For example, for a 2 level model, based on the"
      display "level 2 ID, then the level 1 ID.  You can do this in Stata before"
      display "running this program, or in MLwiN afterwards."


      clear

end

capture program drop makelab
program define makelab
  * variable name, variable number, n of cases, file handle
  args var i n out
  * display "args `var' `i' `n'"

  * CATN 0 c1
  * CATN 1 c1 0 '\male' 1 '\female'

  local vl : value label `var'
  if "`vl'" == "" {
    exit 0
  }

  tempvar lvar
  tempvar first
  decode `var', gen(`lvar')
```

```
  sort `lvar'
  by `lvar' : gen `first' = (_n == 1) & `lvar' != ""

  file write `out' "CATN 0 C`i'" _newline

  local casenum = 1
  while (`casenum' <= `n') {
    if `first'[`casenum'] {
      local v1 = `var'[`casenum']
      local v2 = `lvar'[`casenum']
      file write `out' "CATN 1 C`i' `v1' '\" "`v2'" "'" _newline
    }
    local casenum = `casenum' + 1
  }
  file write `out' _newline
end
```

Stata Program for Analytic Variance

1. Calculate analytic variance using empirical model results

```
global dat "h:\PNAless65\data"

global dta "h:\PNAless65\data"

global pgm "h:\PNAless65\program"

global rlt "h:\PNAless65\result"

global plt "h:\PNAless65\plot"


log using "$rlt\varaa in formula in most AA 3quartile 01222007 final.log", replace
use "$dta\pnaless65.dta",clear
keep if quartile~=1
set type double
g n=1
collapse (count) n, by (site race2)
/*fillin the unexist combination, and define the number of that cell as 0*/
fillin site race2
replace n=0 if n==.
sort  site race2
bysort site:g nwhite= n[1]
bysort site:g naa= n[2]
keep  site naa nwhite
bysort site: keep if _n==1
sort site
save "$dta\3qpnaless65racenumber.dta",replace


use "$dta\pnaless65.dta",clear
keep if quartile~=1

sort site
codebook site


sort site visit


bysort site: g n=_N
bysort site: keep if _n==_N
keep site n
sort site
codebook n
egen M=sum(n)
g  N=_N
g nbar=M/N

g beta_ORI=-2.439
```

```
g beta_AARI=-0.134
g vare_con_RI=0.069


g beta_ORC=-2.415
g beta_AARC=-0.191
g vare_con_RC=0.036
g vare_AA_RC=0.116


g var_RIewhite=2+exp(-(beta_ORI))+exp(beta_ORI)
g var_RIeAA=2+exp(-(beta_ORI+beta_AARI))+exp(beta_ORI+beta_AARI)


g var_RCewhite=2+exp(-(beta_ORC))+exp(beta_ORC)
g var_RCeAA=2+exp(-(beta_ORC+beta_AARC))+exp(beta_ORC+beta_AARC)


g var_u1=vare_AA_RC/N


/*for balanced design of var varAA*/
/*if w is .5*/
g varAA_RIw5=2*(var_RIeAA+var_RIewhite)/M            /*for a*/
g varAA_RCw5=2*(var_RCeAA+var_RCewhite)/M + var_u1  /*for e*/
di "Condition a and d, balance or unbalanced among site with equal sample size of
race"
list varAA_RIw5 varAA_RCw5 in 1/1


sort site
merge site using "$dta\3qpnaless65racenumber.dta"
drop _merge
g wsite=naa/n
save "$dat\3qraw_est.dta", replace



/*if w is the same for each site*/
/*for balanced design of var varAA*/
/*if w is .5 is balanced within and across site case in the col 1*/
forv r=1/9 {
    use "$dat\3qraw_est.dta", clear
    local w=`r'/10
    /*calculate variance of AA in the fixed effect*/
    qui g double varAA_RI`r'=((1-`w')*var_RIeAA+`w'*var_RIewhite)/(`w'*(1-`w')*M)
    /*for b, d*/
    qui g double varAA_RC`r'=((1-`w')*var_RCeAA+`w'*var_RCewhite)/(`w'*(1-`w')*M)
+ var_u1     /*for be*/

    format varAA_RI`r'   varAA_RC`r' %5.3f
```

```
    qui  g double w=`w'

    di "Condition b and e, balance or unbalanced among site and unbalance acroos site
with same weight as " w
    di "var(AA) in fixed effect will be " varAA_RI`r' " in RI and " varAA_RC`r' "
in RC , respecitively."
    di ""
    save "$dat\var_w`i'.dta",replace
    }

/*for balance among site and unbalanced within site design of var varAA, using site
specific weight*/
egen sumw=sum(wsite)
di sumw
    g                                                             double
varAA_RIwsite=((N-sumw)*var_RIeAA+sumw*var_RIewhite)/(nbar*(N-sumw)*sumw)
    /*for b2*/
    g                                                             double
varAA_RCwsite=((N-sumw)*var_RCeAA+sumw*var_RCewhite)/(nbar*(N-sumw)*sumw)       +
var_u1     /*for b2*/
*for unbalance among and within site design of var varAA, using site specific weight*/
g nw=naa
egen sumwn=sum(naa)
di sumwn
g double  varAA_RIwsiten=[(M-sumwn)*var_RIeAA+sumwn*var_RIewhite]/
[(M-sumwn)*sumwn]      /*for b2*/
g double  varAA_RCwsiten=[(M-sumwn)*var_RIeAA+sumwn*var_RIewhite]/
[(M-sumwn)*sumwn] + var_u1     /*for b2*/
    /*calculate power for unbalanced scenario*/
    /*for condition c*/
    di "Condition C, balance among site and unbalance across site with site specific
weight"
    di " var(AA) in fixed effect will be " varAA_RIwsite " in RI, and " varAA_RCwsite
" in RC , respecitively."
/*For conditin f*/
    di "Condition f, unbalance among and across site with site specific weight"
    di "var(AA) in fixed effect will be " varAA_RIwsiten " in RI, and " varAA_RCwsiten
" in RC , respecitively."
ave "$dat\var and power 01182007.dta",replace

log close
print "$rlt\varaa in formula in most AA 3quartile 01222007 final.log"
```

2. **Plot analytic variance using the results from above code**

```
use "F:\PNAless65\data\analytic variance 01232007.dta", clear
label var w "Black%"
label define lw 1 "10%" 2 "20%" 3 "30%" 4 "40%" 5 "50%" 6 "60%" 7 "70%" 8 "80%" 9 "90%" ///
      10 "eqaul cluster site with site specif Balck%" ///
      11 "eqaul cluster site with site specif Balck%" ///
      12 "Use observation"
labe value w lw


label var var "VAR(black)"


label define ldata 1 "Full data" 2 "Q2-Q4"
label data ldata

scatter var w  if  model=="RI" & data==1,  text(0.00473 1 "RI,full data") || ///
     scatter var w  if model=="RC" & data==1, text( 0.00549 1 "RC,full data") || ///
     scatter var w  if model=="RI" & data==2,  text(0.0093  1 "RI,Q2-Q4 data") || ///
     scatter var w  if model=="RC" & data==2,  text(0.0123  1 "RC,Q2-Q4 data") ///
, note("W=10:blanced cluser size with site-spcific weight"  ///
      "W=11:using site-specific Black%" "W=12: using site-specofc information") || ///
line var w  if w <10 & model=="RI" & data==1 ||  line var w  if w <10 & model=="RC" & data==1 || ///
line var w  if w <10 & model=="RI" & data==2 ||  line var w  if w <10 & model=="RC" & data==2,
xlabel( 0 (1) 12) ///
 scheme(s2mono) legend(off) saving("F:\PNAless65\plot\analytic var 01232007.gph", replace)
graph export "F:\PNAless65\plot\analytic var 01232007.emf", replace
graph export "F:\PNAless65\plot\analytic var 01232007.eps", replace
```

B. SAMPLE MLWIN CODE TO FIT UNADJUSTED RI MODEL TO VOLPP STUDY

```
Note: this program use MLwiN2.0(r)
Note: Macros to fit a 2-level logistic random coeffcient model for AA by method RIGLS
PQL2
Note: This is used for Volpp project July 2005 data
Note: I use Stata transfer the String variable and Use do file stata2mlwinlogit
transfer stata data to mlwin obey file
note: I used index to sepcify the order of the observation.


note [A. read in the Volpp pneumonia  younger than 65 years old data]
RETR F:\dec simulation\ws\pnaless65.ws
FPATH C:\Program Files\MLwiN2(r)\discrete
pref pre
post post


note [B. Set Up the Ri or RC model]
note define repsonse variable and level variable

resp    'anysoc30'
iden 2 'site'
iden 1 'visit'
addt   'bcons'
addt   'cons'
addt   'race2'

note: define the contrast matrix to be ready for hypothesis test
joint 0 1 0  c100
name c100 "AAF"

joint 1 0 0   c102
name c102 "INTF"

joint 1 0 0 0 0 c103
name c103 "INTR"



joint 0 0 1 0 0 c101
name c10` "AAR"



note: delcair level-1 variance defining columns linked to G9
link 'bcons'  g9
```

NOTE: Set variance structure at each level
setv 1 'bcons'
setv 2 'cons'   'BLACK'
note [for RI delet 'BLACK' in the level 2 varaince structure]

NOTE: BCONS exists only to specify level 1 variation, so need to remove from fixed
part
fpar 0 'bcons'

note*********************
note: method is RIGLS with pQL2
note*********************

method is RIGLS
note: b10 0 for multinomia and 1 for ordered multinomial
note: b11 0 for 1st order and 0 for 2en order
note: b12 1 for mql and 1 for pql for fixed part
note: b13 0 for logit and 1 for loglog
note: b14 0 for distributional and 1 for unconstrained
note: b16 0 for no mixed model and 1 for yes mixed model
set b10 0
set b11 2
set b12 1
set b13 0
set b14 0
set b15 1
set b16 0

NOTE: Run model to convergence
batc 1
note [C. Run the model]
start

note [D. Copy emprical parameter estimate from specific column to a new columm to
aviod the raw parameter estimate]
calc c106=c1096
calc c107=c1097
calc c108=c1098
calc c109=c1099

note [E. Erase Column C1096-c1099]
erase c1096-c1099

note [save this worksheet containn the parameter estimates for the Volpp data]
save F:\dec simulation\rawresult\pnaless65rc_raw.ws

echo 1

note: [store the corresponding parameter estimates and hypothesis test in a txt file]

logon F:\dec simulation\rawresult\pnaless65rc_raw.txt
fixed note [save the fixed effect estimates]
random note [save the random effect estimates]
RTEST C101 note [do a hypothesis on defined contrast matrix, here for random effect
for Blakc]
rtest c103 note [random effect test on intercept residual]
ftest c100 note [fixed effect test on Black as fixed effect]
ftest c102 note [fixed effect test on intercept term]
logo

C. SAMPLE MLWIN CODE TO RUN SIMULATION ON 2-LEVEL MODEL

```
note [get the Volpp worksheet]
retr D:\Dec simulation\raw_ws\pnaless65_RI_raw_SIMU.ws
 note this simulate response variable should refer to multilevel archieve 1025
pause 2
Note[when simulate power, we can modify the beta 1 by add edit 2 c108 -0.1 in the
next line]
erase c500-c517
 note [clear columns that will hold simulation results]
BATCh  1
 note [run each simulation rep until convergence]
MAXIterations 50
 note [but do not  run more than 50 iterations per simulation replicate]
loop  b50 1 2000
    note [Do below loops (T=2000) times ]
note [A. Assign initial parameter estimates in column C1096-c1099 from C106-c109]
  calc c1096=c106
  calc c1097=c107
  calc c1098=c108
  calc c1099=c109
note  [B. Simulate estimate of random effects]
  simu 2  C500
note  [C. Simulate estimate of fixed effect]
  pred  C501
note [D & E. Calculate the probability of response ,pi= anti-log(XB+ZU)]
  calc  C502 = alog (C500+C501)
Note [F. Simulate the new binary response variable from bin(n, pi)]
  bran 37111 C503  C502  'denom'
Note [G. Fit the RI or RC model with this simulated response variable]
note [Modify response variable to the new simulated response variable]
resp c503
note [run the simulation replicate]
star
join c511 c1096 c511
note [stack variances of random effects in c511]
join c512 c1098 c512
note [stack beta's in c512]
joint c513 b50 c513
echo 1

note [H. Conduct the hypothesis test for the fixed and or random effect of black
race and save the statistics results]
note D:\Dec simulation\simu\ri\betahat\simuresults\PNALESS65_TESTSITEF_ri_lap.txt
logo D:\Dec simulation\simu\ri\betahat\simuresults\PNALESS65_TESTSITEF_ri_lap.txt
```

note beta is beta hat
FTEST 'SITE_F'
logo

note loga D:\Dec simulation\simu\ri\betahat\simuresults\PNALESS65_TESTAAF_ri_
lap.txt
logo D:\Dec simulation\simu\ri\betahat\simuresults\PNALESS65_TESTAAF_ri_lap.txt
note beta is beta hat
FTEST 'AA_F'
logo

note loga D:\Dec simulation\simu\ri\betahat\simuresults\PNALESS65_TESTSITER_ri_
lap.txt
logo D:\Dec simulation\simu\ri\betahat\simuresults\PNALESS65_TESTSITER_ri_lap.txt
RTEST 'SITE_R'
logo

note [I. Store Parameter estimate]
NOTE: BEFORE RUN THE SIMULATION, I NEED CREATE BELOW FILE BY MYSELF or using logo
note [the first loop will use logo and the other use loga]
note loga D:\Dec simulation\simu\ri\betahat\simuresults\par_est_ri_lap.txt
logo D:\Dec simulation\simu\ri\betahat\simuresults\par_est_ri_lap.txt
note beta is beta hat
fixed
random
logo

note finished one loop
echo 0
endloop

NOTE SAVE RELATED SIMULATION RESULTS FOR FURTHER ANALYSIS
SAVE D:\Dec simulation\simu\ri\betahat\SIMUWS\PNALESS65ri_SIMU.WS

Sample SAS and Stata Program to Analyze Simulation Results

1. SAS Macro to Read and analysis Simulation Results

```
PROC PRINTTO LOG="D:\Dec simulation\simu\CALCULATE VAR OF BLACK AS FIXED EFFECT
LOG.TXT"
                        PRINT="D:\Dec simulation\simu\CALCULATE  VAR OF BLACK AS
FIXED EFFECT OUTCOME.TXT";
***********READ IN VARIANCE FOR BETA HAT********************;
%MACRO VARAABETAHAT(TYPE= );
LIBNAME  &TYPE.HAT  "D:\Dec simulation\simu\&TYPE.\betaHAT\simuanalysis";
DATA  &TYPE.HAT.VARAAF&TYPE.BETAHAT;
 INFILE "D:\Dec
simulation\simu\&TYPE.\betaHAT\simuresults\par_est_&TYPE._LAP.TXT";
    INPUT  RACE  $  1-5 @ ;
        IF RACE='Black';
            INPUT EST 25-34  SE 35-45;
VARAA=SE**2;
TYPE="&TYPE";
BETA="BHAT";
TITLE "SAMPLE VARIANCE OF VAR(BLACK) FOR &TYPE MODEL AND SIMULATED ON BETA HAT ";
PROC MEANS; VAR VARAA;RUN;
%MEND;


***************WHEN BETA LARGE THAN THAN 0**************************;
%MACRO VARAABETA(TYPE=, BETAHO= );
%DO i=1 %TO &BETAHO;
LIBNAME CHEN&TYPE.&I "D:\Dec simulation\simu\&TYPE.\beta&I.\simuanalysis";

DATA CHEN&TYPE.&I..VARAAF&TYPE.&I;
 INFILE "D:\Dec
simulation\simu\&TYPE.\beta&I.\simuresults\par_est_&TYPE._HOME.TXT";
    INPUT  RACE  $  1-5 @ ;
        IF RACE='Black';
            INPUT EST 25-34  SE 35-45;
VARAA=SE**2;
TYPE="&TYPE";
BETA="&I";
TITLE "SAMPLE VARIANCE OF VAR(BLACK) FOR &TYPE MODEL AND SIMULATED ON BETA=&I ";
PROC MEANS; VAR VARAA;RUN;
%END;
%MEND;


***************WHEN BETA LESS THAN 0**********************;
%MACRO VARAABETA_(TYPE=, BETAHO=);
%DO i=1 %TO &BETAHO;
```

```
LIBNAME CHEN&TYPE._&I "D:\Dec simulation\simu\&TYPE.\beta_&I.\simuanalysis";

DATA CHEN&TYPE._&I..VARAAF&TYPE._&I;
 INFILE "D:\Dec
simulation\simu\&TYPE.\beta_&I.\simuresults\par_est_&TYPE._HOME.TXT";
    INPUT  RACE  $  1-5 @ ;
        IF RACE='Black';
            INPUT EST 25-34  SE 35-45;
VARAA=SE**2;
TYPE="&TYPE";
BETA="-&I";
TITLE "SAMPLE VARIANCE OF VAR(BLACK) FOR &TYPE MODEL AND SIMULATED ON BETA=-&I ";
PROC MEANS; VAR VARAA;RUN;
%END;
%MEND;


%VARAABETAHAT(TYPE=RI);
%VARAABETA(TYPE=RI, BETAH0=9);
%VARAABETA_(TYPE=RI, BETAH0=9);


%VARAABETAHAT(TYPE=RC);
%VARAABETA(TYPE=RC, BETAH0=5);
%VARAABETA_(TYPE=RC, BETAH0=5);


PROC PRINTTO;RUN;



/*SET ALL THE VARIANCE TOGETHER*/
%MACRO ALLVAR_(TYPE=, BETAH0=);
%DO i=1 %TO &BETAH0;
LIBNAME CHEN&TYPE._&I "D:\Dec simulation\simu\&TYPE.\beta_&I.\simuanalysis";
DATA VARALL; SET VARALL CHEN&TYPE._&I..VARAAF&TYPE._&I ;
RUN;
%END;
%MEND;


%MACRO ALLVAR(TYPE=, BETAH0=);
%DO i=1 %TO &BETAH0;
LIBNAME CHEN&TYPE.&I "D:\Dec simulation\simu\&TYPE.\beta&I.\simuanalysis";
DATA VARALL; SET VARALL CHEN&TYPE.&I..VARAAF&TYPE.&I ;
RUN;
%END;
%MEND;
```

```
DATA VARALL; SET _NULL_;
%ALLVAR(TYPE=RI, BETAH0=9);RUN;
%ALLVAR_(TYPE=RI, BETAH0=9);
%ALLVAR(TYPE=RC, BETAH0=5);
%ALLVAR_(TYPE=RC, BETAH0=5);RUN;
DATA ALLVAR; SET VARALL RIHAT.VARAAFRIBETAHAT RCHAT.VARAAFRCBETAHAT ;
RUN;
LIBNAME SIMU "D:\Dec simulation\simu\";
DATA SIMU.ALLVAR; SET ALLVAR;
TITLE "COMBO DATA SET FOR VAR UNDER DIFFERENT MODEL AND BETAH0";
PROC CONTENTS; RUN;
```

2. Sample Stata Program to get Histogram plot of simulated variance for the fixed effect of black race.

```
use "D:\Dec simulation\simu\SAS to analysis power and variance for black\allvar.
dta",clear
histogram varaa if type=="RI" & beta=="BH",  xline(0.0023) ///
       text(5000 0.0024 "0.0023") kdensity note("variance(black), RI model")
saving("c:\ri_1.gph", replace)
graph export "c:\ri_1.eps",replace
```

3. Sample Stata program to plot cumulative distribution

```
use "D:\Dissertation\09282006\PNAless65\data\PNA with Quatile in PNA and ALL site
level.dta", clear
sort site
cumul naa, gen(cumnaa)
cumul nwhite , gen(cumnwhite)
summ cumnaa cumnwhite
stack cumnaa naa cumnwhite nwhite , into(cumu npat) wide clear
label var cumnaa  "Black"
label var cumnwhite "White"
label var naa  "Black"
label var nwhite "White"
line cumnaa cumnwhite npat, sort scheme(s2mono) xtitle("Site and Race Specific
Patient Number")  ///
    xlabel(0 (100) 600)  ytitle("Proportion")
*graph export "I:\stataPNAless65\plot\Acumuaa.eps",replace
graph export "D:\Dissertation\Pctex draft\2007\Apr2007\Acumuaa.eps",replace
graph export "D:\Dissertation\Pctex draft\2007\Apr2007\cumufull.eps",replace
graph export "G:\Acumuaa.eps",replace
graph export "G:\cumufull.eps",replace



use "D:\Dissertation\09282006\PNAless65\data\PNA with Quatile in PNA and ALL site
level.dta", clear
keep if quartile>1
sort site
cumul naa, gen(cumnaa)
cumul nwhite , gen(cumnwhite)
summ cumnaa cumnwhite
stack cumnaa naa cumnwhite nwhite , into(cumu npat) wide clear
label var cumnaa  "Black"
label var cumnwhite "White"
line cumnaa cumnwhite npat, sort scheme(s2mono)  xtitle("Site and Race Specific
```

Patient Number") ///
    xlabel(0 (100) 600)   ytitle("Proportion")
*graph export "I:\stataPNAless65\plot\Acumuaa.eps",replace
graph export "D:\Dissertation\Pctex draft\2007\Apr2007\Q24Acumuaa.eps",replace
graph export "D:\Dissertation\Pctex draft\2007\Apr2007\cumuq24.eps",replace
graph export "G:\Q24Acumuaa.eps",replace
                    graph export "G:\cumuq24.eps",replace

Main Effect 2-level RI Model in Stata

Full Population

```
. xtlogit  anysoc30 race2, fe i(site)

note: multiple positive outcomes within groups encountered.

note: 5 groups (73 obs) dropped due to all positive or
      all negative outcomes.

Iteration 0:   log likelihood = -9418.3992

Iteration 1:   log likelihood = -9418.3985

Conditional fixed-effects logistic regression   Number of obs     =     37038

Group variable (i): site                        Number of groups  =       144

                                                Obs per group: min =        20

                                                            avg =     257.2

                                                            max =       921

                                                LR chi2(1)        =      5.66

Log likelihood  = -9418.3985                    Prob > chi2       =    0.0173
```

anysoc30	Coef.	Std. Err.	z	P>|z|	[95% Conf. Interval]	
race2	-.118133	.0498915	-2.37	0.018	-.2159186	-.0203475

For Q2-Q4 sum-sample

```
. xtlogit  anysoc30 race2 if  quartile!=1, fe i(site)

note: multiple positive outcomes within groups encountered.

Iteration 0:   log likelihood = -4756.9018

Iteration 1:   log likelihood = -4755.7606

Iteration 2:   log likelihood = -4755.7606


Conditional fixed-effects logistic regression   Number of obs     =     17957

Group variable (i): site                        Number of groups  =        42


                                                Obs per group: min =        73

                                                            avg =     427.5

                                                            max =       921

                                                LR chi2(1)        =      2.95

Log likelihood  = -4755.7606                    Prob > chi2       =    0.0860
```

anysoc30	Coef.	Std. Err.	z	P>|z|	[95% Conf. Interval]	
race2	-.1027182	.0599554	-1.71	0.087	-.2202286	.0147922

Conditional Logistic Model with Race*Site Interaction
(Partial Result with Notations)

****

For Over all 149 site race*site interaction Conditional logistic model

****

. xi: xtlogit anysoc30 i.site*race2 , i(site) fe

i.site   _Isite_1-150   (naturally coded; _Isite_1 omitted)

i.site*race2   _IsitXrac_#   (coded as above)

note: _IsitXrac_2 dropped due to collinearity

···(8 interaction dropped due to collinearity)

note: multiple positive outcomes within groups encountered.

note: 5 groups (73 obs) dropped due to all positive or

     all negative outcomes.

note: _Isite_2 omitted due to no within-group variance.

··· omit

note: _Isite_150 omitted due to no within-group variance.

(All 148 site, except reference site omitted due to no within group variance)

note: _IsitXrac_18 omitted due to no within-group variance.

..

note: _IsitXrac_88 omitted due to no within-group variance.

(4 interaction omitted due to within group variance)

Iteration 0:   log likelihood = -9421.2307

···

Iteration 14: log likelihood = -9342.7467

Conditional fixed-effects logistic regression	Number of obs	=	37038
Group variable (i): site	Number of groups	=	144

	Obs per group: min =	20
	avg =	257.2
	max =	921

	LR chi2(136)	=	156.97
Log likelihood = -9342.7467	Prob > chi2	=	0.1054

----

anysoc30	Coef.	Std. Err.	z	P>|z|	[95% Conf. Interval]
race2	-15.12217	5407.648	-0.00	0.998	-10613.92 10583.67
..
_IsitXrac_7	15.57837	5407.648	0.00	0.998	-10583.22 10614.37
_IsitXrac_8	13.61087	5407.648	0.00	0.998	-10585.18 10612.41
_IsitXrac_9	14.5775	5407.648	0.00	0.998	-10584.22 10613.37

…omitted… due to uniform cases the parameter estimate are not reliable with infinite OD and SE

_____

. testparm _IsitXrac_*

(1) [anysoc30]_IsitXrac_3 = 0

…omit

 (136) [anysoc30]_IsitXrac_150 = 0

          chi2(136) = 110.49

        Prob > chi2 =   0.9468

```
*********************************************************
For Q2-Q4 race*site interaction Conditional logistic model
*********************************************************
. xi: xtlogit  anysoc30 i.site*race2 if quartile!=1, i(site) fe

i.site            _Isite_1-150        (naturally coded; _Isite_1 omitted)

i.site*race2      _IsitXrac_#         (coded as above)

note: _Isite_2 dropped due to collinearity

…

note: _Isite_150 dropped due to collinearity (107 dropped due to collinearity by if quartile!=1)

… omit

note: _IsitXrac_150 dropped due to collinearity(107 dropped due to collinearity by if quartile!=1)

note: multiple positive outcomes within groups encountered.

note: _Isite_15 omitted due to no within-group variance.

…

note: _Isite_148 omitted due to no within-group variance. (41 site main effect omitted due to no within-group
variance)

Iteration 0:   log likelihood = -4735.8498

… omit

Iteration 4:   log likelihood = -4722.7491
```

Conditional fixed-effects logistic regression	Number of obs	=	17957
Group variable (i): site	Number of groups	=	42
	Obs per group: min =		73
	avg =		427.5
	max =		921
	LR chi2(42)	=	68.97
Log likelihood = -4722.7491	Prob > chi2	=	0.0054

```
------------------------------------------------------------------------------
    anysoc30 |     Coef.   Std. Err.      z    P>|z|    [95% Conf. Interval]
-------------+----------------------------------------------------------------
       race2 |  .5622971   .7294469     0.77   0.441   -.8673926    1.991987
 _IsitXrac_15 | -.8058547   .7997266    -1.01   0.314    -2.37329    .7615807
 _IsitXrac_16 | -.9836094   .8355352    -1.18   0.239   -2.621228    .6540094
 _IsitXrac_17 |  -.966049   .8237389    -1.17   0.241   -2.580548    .6484496
 _IsitXrac_24 |  .1510563   .7863994     0.19   0.848   -1.390258    1.692371
 _IsitXrac_27 | -.7577912   .8926936    -0.85   0.396   -2.507439    .9918561
 _IsitXrac_28 | -1.150195   1.025168    -1.12   0.262   -3.159487    .8590965
 _IsitXrac_35 |  -.007033   .8185346    -0.01   0.993   -1.611331    1.597265
 _IsitXrac_36 | -1.452956   1.154151    -1.26   0.208    -3.71505    .8091389
 _IsitXrac_37 |  .0208832   1.040516     0.02   0.984   -2.018492    2.060258
 _IsitXrac_38 | -.5968326   .9099023    -0.66   0.512   -2.380208    1.186543
 _IsitXrac_39 | -1.672837   .9079882    -1.84   0.065   -3.452461    .1067875
 _IsitXrac_41 | -.1971283   .8000676    -0.25   0.805   -1.765232    1.370975
 _IsitXrac_43 | -.8101344   .8217179    -0.99   0.324   -2.420672    .8004031
```

_IsitXrac_44	−1.074545	.8385114	−1.28	0.200	−2.717997	.5689073
_IsitXrac_46	−.6071161	.7799462	−0.78	0.436	−2.135783	.9215504
_IsitXrac_49	−.1400908	.8945042	−0.16	0.876	−1.893287	1.613105
_IsitXrac_54	−.2369969	.8085899	−0.29	0.769	−1.821804	1.34781
_IsitXrac_55	−.8024249	.883466	−0.91	0.364	−2.533986	.9291367
_IsitXrac_59	−.8175974	.9568776	−0.85	0.393	−2.693043	1.057848
_IsitXrac_66	−.7069955	.8138557	−0.87	0.385	−2.302123	.8881324
_IsitXrac_68	−.4545023	.7656105	−0.59	0.553	−1.955071	1.046067
_IsitXrac_70	−1.620942	.9078022	−1.79	0.074	−3.400202	.1583171
_IsitXrac_73	−.3058474	.7909994	−0.39	0.699	−1.856178	1.244483
_IsitXrac_74	−1.123635	.849642	−1.32	0.186	−2.788903	.5416324
_IsitXrac_85	−.4046785	.8327242	−0.49	0.627	−2.036788	1.227431
_IsitXrac_86	−1.476774	.8802326	−1.68	0.093	−3.201998	.2484501
_IsitXrac_87	−.9152808	.9157872	−1.00	0.318	−2.710191	.8796292
_IsitXrac_95	−.3096814	.7926688	−0.39	0.696	−1.863284	1.243921
_IsitXrac_97	−.2853455	.8628361	−0.33	0.741	−1.976473	1.405782
_IsitXra~102	−1.275098	.8846968	−1.44	0.150	−3.009072	.4588757
_IsitXra~104	−.798853	.8193812	−0.97	0.330	−2.404811	.8071046
_IsitXra~105	−.4904095	.9410685	−0.52	0.602	−2.33487	1.354051
_IsitXra~114	−.4413513	.8614307	−0.51	0.608	−2.129724	1.247022
_IsitXra~116	−.6687789	.8991715	−0.74	0.457	−2.431123	1.093565
_IsitXra~121	−.4302093	.776076	−0.55	0.579	−1.95129	1.090872
_IsitXra~125	−1.936477	.8479484	−2.28	0.022	−3.598425	−.2745287
_IsitXra~129	−1.502887	.8860319	−1.70	0.090	−3.239477	.2337039
_IsitXra~133	−.0337316	.8521558	−0.04	0.968	−1.703926	1.636463
_IsitXra~139	.1636542	.8297453	0.20	0.844	−1.462617	1.789925
_IsitXra~146	−.9067121	.8902018	−1.02	0.308	−2.651476	.8380515
_IsitXra~148	−1.16748	.7736773	−1.51	0.131	−2.683859	.3488998

. testparm _IsitXrac_*

 (1) [anysoc30]_IsitXrac_15 = 0

··· omit other terms···

(41) [anysoc30]_IsitXrac_148 = 0

          chi2(41) =   60.71

        Prob > chi2 =   0.0243 ➔ there exist site and race interaction

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