

A Review on Logistic Regression in Medical Research

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ABSTRACT

In today's scenarios many healthcare decisions are being taken by predictive modelling and machine learning techniques. With this review, we focused on logistic regression model, a kind of predictive modelling used in machine learning, and how healthcare researchers take decisions by the help of predictive modelling. For a better data analysis in healthcare, we need to understand the concept of logistic regression as well as others terms, which are linked with it. so that we can clearly understand the concept behind it and implement in medical research. In this review we worked on an example and illustrated how to perform logistic regression using R programming language. The aim of this paper is to understand logistic regression in healthcare and implement it for decision making.

Key words: Logistic regression, Odds ratio, R programming

INTRODUCTION

Logistic regression (LR) modelling is now an popular statistical tool in healthcare analysis and medical research, from last three decades.¹ its origin was established in 19th century², It is the most common statistical method to predict the dichotomous dependent variable using one or more than one independent variables.^{3,4,5} The French mathematician Pierre François Verhulst invented logistic function in 19th century for the description of growth of human populations.⁶ In between 1838 to 1847 Verhulst published his suggestions which were edited by Quetelet.⁷ Pearl and Reed discovered a new logistic function in 1920 in USA for a study of the population growth.⁸ Logistic regression (LR) is used when the dependent variable in the study is dichotomous and contains factor like decision making (yes or no), disease state (diseased or healthy). Some complex form of logistic regression can be solved using multinomial regression analysis, where predict variable takes more than two categories.^{9,10} In order to fit a model, certain assumptions are made. but in case of logistic

regression model, it does not assume a kind of linear relationship between the dependent variable and independent variables.¹⁰ In most of the research analysis logistic regression can be used to deduce how the independent variables are affecting the dependent variable in a particular study.^{11,14,15} for example we may consider in a healthcare the patient will die or survive after an intervention.^{12,13} whether a new born baby will be overweight or underweight. So, for this kind of prediction purpose the LR model can be used.

MATERIALS AND METHODS

2.1. The Logistic Regression Model

The logistic equation is given by

$$(Y) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 x_1)}} = \frac{e^{(\beta_0 + \beta_1 x_1)}}{1 + e^{(\beta_0 + \beta_1 x_1)}} \dots\dots\dots (1)$$

When there are several predictors in the data, the equation becomes:

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$$P(y) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \dots + \beta_i x_i)}} \dots\dots\dots(2)$$

$$= \frac{e^{(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \dots + \beta_i x_i)}}{1 + e^{(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \dots + \beta_i x_i)}} \dots\dots\dots(3)$$

Where

$\beta_0, \beta_1, \beta_2, \beta_i$ are the coefficient of regression equation

And x_1, x_2, x_3, x_i are the independent variables in the given equation.

a “link function” that links the Dependent variable and independent variable is

$$\ln\left[\frac{\pi_i}{1-\pi_i}\right] = \frac{e^{(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_i x_i)}}{1 + e^{(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_i x_i)}} \dots\dots\dots(4)$$

Now we can write the above equation as

$$\left[\frac{\pi_i}{1-\pi_i}\right] = e^{(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_i x_i)} \dots\dots\dots(5)$$

Now solving equation (5) we can find out our required equation i.e equation (3)

2.2 Introduction to Logistic Curve

In logistic regression model the outcome variable takes the value 0 and 1 and the predicted values falls within the range 0 and 1, as we know the total probability is always 1. logistic regression uses the logistic curve to find out relationship between the independent and outcome variable. The probability follows 0, At very low values of the independent variable, never reaches 0. and if the independent variable increases the logistic regression curve approaches towards 1. But never equal to 1.

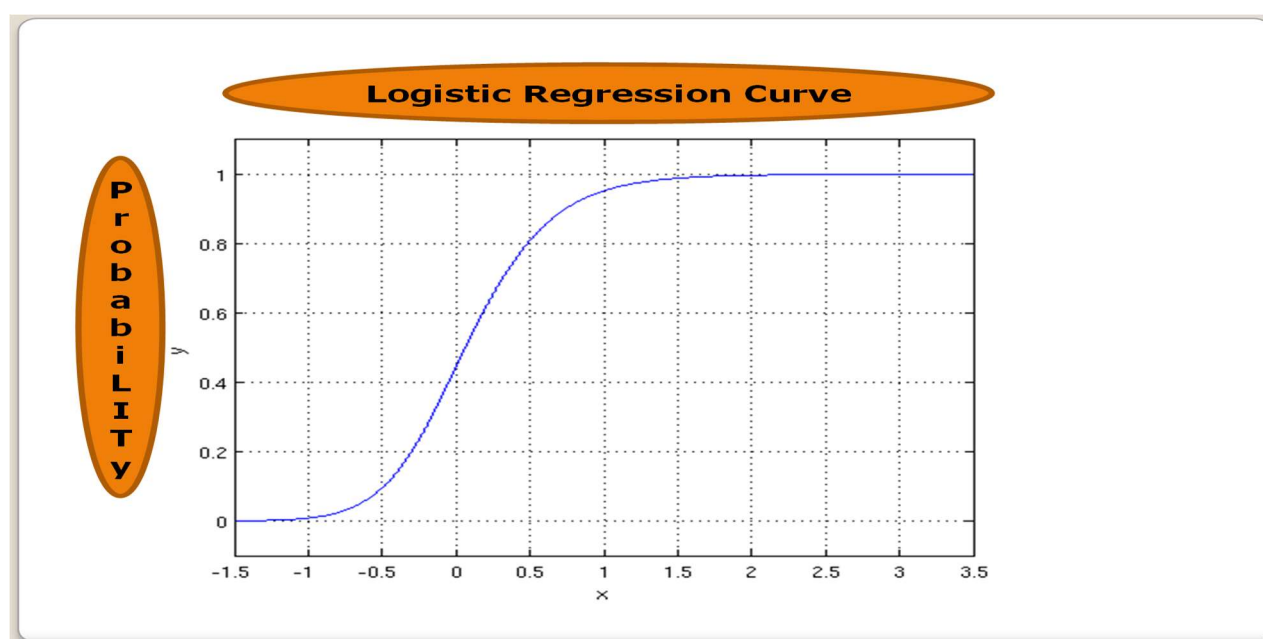


Fig 1: The curve of logistic regression

2.3 Converting a Probability into Odds and Logit Values

The estimated values, which are given by logistic regression model, do not fall outside the range of 0 and 1. we can obtain this by two step methods. firstly, we can restate the probability as odds, which can be defined as the ratio of probability of occurring with probability of non-occurring. for example, for example, if a doctor has a probability of 0.7 to succeed in a certain operation, then the odds of success are 0.7/(1-0.7).

3. Introduction to R programming Language

According to the survey in 2021, R programming language is a widely used and most preferable statistical language. Now a day's R programming language is an emerging programming language. Many health care researchers are using this for data management,

data cleaning, data preparation and data analysis. It has many statistical functions, which are very easy to use. it contains a large library, which enables the researchers to prefer this language. Many complex graphics, bivariate plots, 3D plots can be drawn using this language. so here in this paper we used the R programming language to implement a working example of logistic regression.

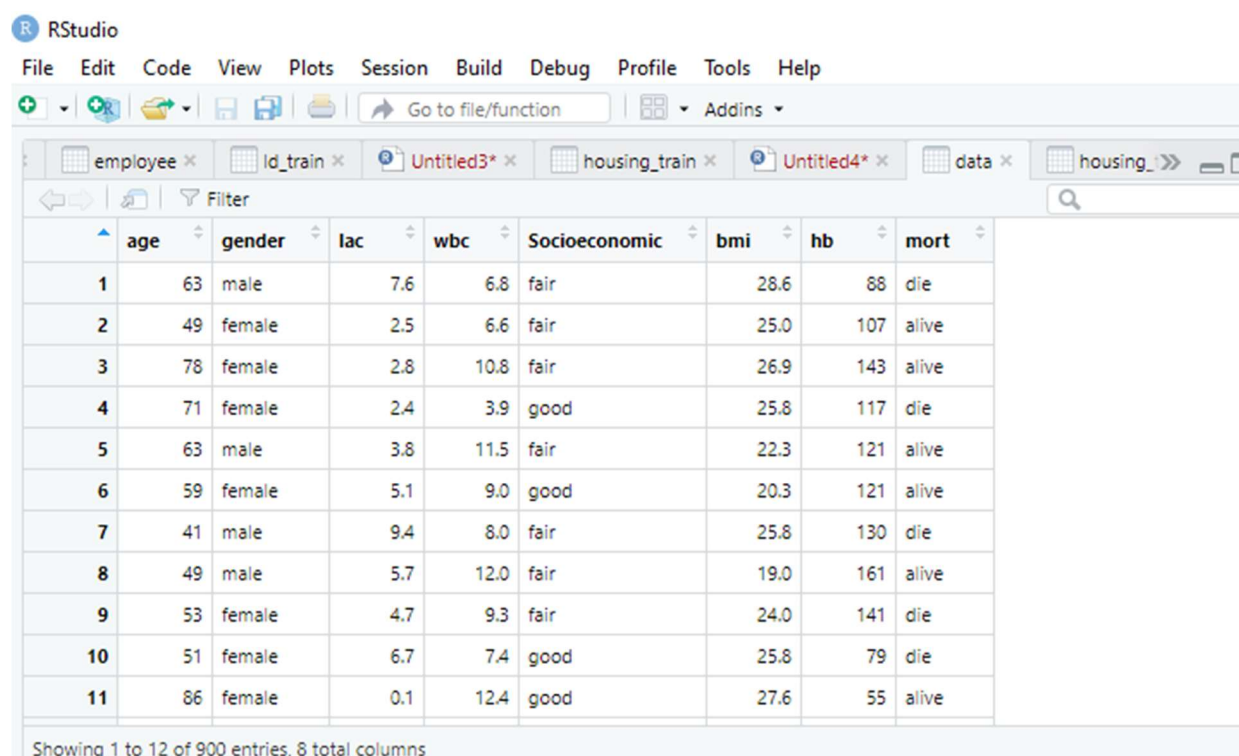
3.1 Working example of Logistic Regression using R Studio

Here in this working example, to show the application of logistic regression, we have created some variables using R studio. Our objective was to show the factors affected mortality using modelling. in this example, we have considered 7 independent variables to predict the mortality of the patient.

```

set.seed(999)
#age of the patients
age<-abs(round(rnorm(n=900, mean=67, sd=14)))
#socioeconomic status of the patients
Socioeconomic<-factor(rbinom(n=900, size=1, prob=0.6), labels=c("good", "fair"))
#bmi of the patients
bmi<-abs(round(rnorm(n=900, mean=25, sd=2.5), 1))
#lac of the patients
lac<-abs(round(rnorm(n=900, mean=5, sd=3), 1))
# gender of the patients
gender<-factor(rbinom(n=900, size=1, prob=0.6), labels=c("male", "female"))
# wbc scores of the patients
wbc<-abs(round(rnorm(n=900, mean=10, sd=3), 1))
# hb of the patients
hb<-abs(round(rnorm(n=900, mean=120, sd=40)))
# Calculating z value
z<-0.1*age-0.02*hb+lac-10
pr = 1/(1+exp(-z))
y = rbinom(900, 1, pr)
#mortality of the patients
mort<-factor(rbinom(900, 1, pr), labels=c("alive", "die"))
#creating data frame
data<-data.frame(age, gender, lac, wbc, Socioeconomic, bmi, hb, mort)

```



	age	gender	lac	wbc	Socioeconomic	bmi	hb	mort
1	63	male	7.6	6.8	fair	28.6	88	die
2	49	female	2.5	6.6	fair	25.0	107	alive
3	78	female	2.8	10.8	fair	26.9	143	alive
4	71	female	2.4	3.9	good	25.8	117	die
5	63	male	3.8	11.5	fair	22.3	121	alive
6	59	female	5.1	9.0	good	20.3	121	alive
7	41	male	9.4	8.0	fair	25.8	130	die
8	49	male	5.7	12.0	fair	19.0	161	alive
9	53	female	4.7	9.3	fair	24.0	141	die
10	51	female	6.7	7.4	good	25.8	79	die
11	86	female	0.1	12.4	good	27.6	55	alive

Showing 1 to 12 of 900 entries, 8 total columns

Fig 2: Preparation of data frame using R studio

3.2 Step one: Univariate data analysis using R

To find out the unadjusted link between outcome and independent variables we perform an univariate data analysis of our data. We separately included each of the independent variable to our model.

```

# univariate analysis for age .....
univariate.age<-glm(mort~age, family = binomial)
summary(univariate.age)
# univariate analysis for Socioeconomic status.....
univariate.Socioeconomic<-glm(mort~Socioeconomic, family = binomial)
summary(univariate.Socioeconomic)

```

Table 1 Results of Univariate data analysis

Variable	Coefficient	Standard error	Z value	P value
Age	0.042012	0.005505	7.631	<0.000
Socioeconomic	-0.1807	0.1381	-1.308	0.191
bmi	0.01263	0.02730	0.463	<0.000
lac	0.81361	0.05343	15.23	<0.000
gender	-0.23938	0.13882	-1.724	0.0846
wbc	0.007481	0.022465	0.333	0.739
hb	-0.009103	0.001721	-5.289	<0.000

Logistic Regression is generalized linear model in R [16]. The result of the univariate regression can be access through the summary () function. if a p value is less than 0.25, we can include those variables for further analysis for clinical relevance. [17, 18]. Now from table 1 we can observe that four variables age, bmi, lac, hb are statistically significant ($p < 0.05$) in univariate analysis. But for clinical relevance we shall include all the variables in further analysis.

3.3 Step two: multivariate model comparisons using R

Here in this step, we fitted two logistic regression model i.e. model 1 and model2 to analyze our data set. From the first model it is observed that the variables socioeconomic status, gender,wbc are insignificant($p > 0.05$).whereas the factors age ,bmi ,lac,hb are statistically significant($p < 0.05$).

Hence to create more accurate model, we exclude the insignificant variables like socioeconomic status,gender,wbc from our model and created a new model i.e. model2.Now by observing the result we can verify that all the factors in model 2 are statistically significant.

#Multivariate data analysis

```
model1<- glm(mort~lac+hb+wbc+age+bmi+Socioeconomic+gender, family = binomial)
```

```
summary(model1)
```

Call:

```
glm(formula = mort ~ lac + hb + wbc + age + bmi + Socioeconomic + gender, family = binomial)
```

```
      Min       1Q   Median       3Q      Max
-2.64350 -0.40850 -0.09155  0.39316  3.10143
```

Table 2: Results of Model 1

Coefficients:	Estimate	Std. Error	Z value	Pr(> z)
Intercept	-10.228369	1.382006	-7.401	1.35e-13***
lac	1.037040	0.071166	14.572	<2e-16***
hb	-0.019164	0.002885	-6.643	3.08e-11***
wbc	-0.008139	0.035393	-0.230	0.818
age	0.094568	0.009808	9.642	<2e-16***
bmi	0.037173	0.042619	0.872	<2e-16***
Socioeco	-0.229991	0.219703	1.047	0.295
gender	-0.340773	0.224199	-1.520	0.129

Null deviance: 1234.19 on 899 df

Residual deviance: 564.42 on 892 df

AIC: 580.42

Now from the above analysis we can see that the factors wbc, bmi, Socioeconomic status and gender are not statistically significant ($p > 0.05$). Hence, we shall create another model by removing these three variables and create model 2.

Call:

```
glm(formula = mort ~ lac + hb + age + bmi + gender, family = binomial)
```

Deviance Residuals:

```
      Min       1Q   Median       3Q      Max
-2.66375 -0.41459 -0.09164  0.38986  3.05810
```

Table 3: Results of Model2

Coefficients:	Estimate	Std. Error	Z value	Pr(> z)
Intercept	-10.349741	1.352668	-7.651	1.99e-14***
lac	1.036494	0.071090	14.580	<2e-16***
hb	-0.019219	0.002882	-6.668	3.08e-11***
age	0.093628	0.009736	9.617	<2e-16***
bmi	0.035833	0.042603	0.841	<2e-16***

Null deviance: 1234.19 on 899 df

Residual deviance: 565.56 on 894 df

AIC: 577.56

Number of Fisher Scoring iterations: 6

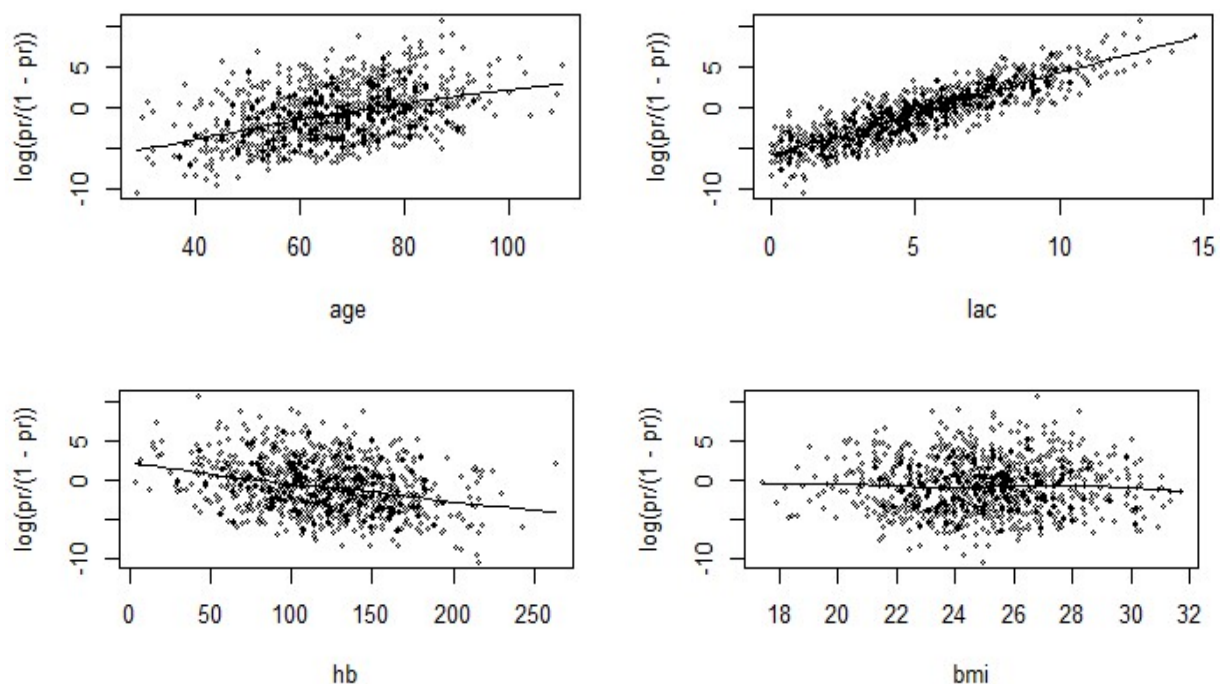
Now we found a better result in model 2.all the variables associated with mortality are statistically significant ($p < 0.05$). Also we can extract the estimated coefficients from fitted model using the function `coef()`.Now we compared model1 with model2 by using partial likelihood ratio test.

```
#initiate library lmttest
library(lmttest)
lrtest(model1,model2)
Model 1: mort ~ lac + hb + wbc + age + bmi + Socioeconomic + gender
Model 2: mort ~ lac + hb + age + bmi
#Df LogLik Df Chisq Pr(>Chisq)
1 8 -282.21
2 6 -282.78 -2 1.142 0.565
```

Now from the above result the chi-square value (0.565) indicates that there is no difference between model1 and model2 according to fit of the data. we can say model2 is a good model as all the independent variables are significant($p < 0.05$) .

3.4 Step three: Test of linearity using R

Here we considered the four independent variable which are statistically significant for the outcome variable. To test the linearity of these variable to the logit of the outcome, we used scatter. Smooth function.

**Fig 3: Test of linearity**

Now from the above graphics we can see that the significant variables in model2 linearly associated with mortality outcome in logit scale (Figure 3). In case the smooth scatter plot shows nonlinearity, we can use alternative method to build our model.

3.5 Step four models fitting using R

Finally, we checked the fit of our model. We examined if there is any significant difference between obtained data and fitted data. We can check the model fit in two ways. Firstly, the model fit can be checked by using goodness of fit (GOF). Secondly by using regression diagnostics plot. We shall verify the fit of the model. The most common method for model fit is Hosmer-Lemeshow test. We performed the Hosmer-Lemeshow test in R and the results are shown below. Here from the table, we can observe that the p value is 0.069, which indicates there is no significant difference between observed and predicted values.

Table 4: Test of goodness of fit

Step	Chi-square	sig
1	14.23	.069

DISCUSSION

We have seen how to model a continuous numeric response with linear regression technique. But in many healthcare scenarios our target is binary. In medical research most of the classification problems are dealt by LR model. In this paper, we considered a working example to predict mortality of the patient. We created a data frame by using R programming language and finally we ended with performing a suitable logistic regression model. Now this data will be considered as “train” data, as we used this data to create our model. Now the performance of the model can be tested by using a “test” data, which has not been delivered in this paper. Most of the study does not focus on diagnosis plot, fit of the model and validation of the model [16] [17], while building a LR model, we have to take care of these things to create an accurate model.

CONCLUSION

In this paper we discussed the role of logistic regression in healthcare research. As it is a machine learning technique many researchers are using this as a predictive modelling algorithm. Apart from this R programming language is an emerging programming language, which is used in healthcare research for predictive modelling. This study put a light on how to build logistic regression model using R programming language. And finally, we checked linearity of the data, fit of the model, which are very essential for model building.

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Randomization Does Not Justify Logistic Regression

David A. Freedman

Abstract. The logit model is often used to analyze experimental data. However, randomization does not justify the model, so the usual estimators can be inconsistent. A consistent estimator is proposed. Neyman’s non-parametric setup is used as a benchmark. In this setup, each subject has two potential responses, one if treated and the other if untreated; only one of the two responses can be observed. Beside the mathematics, there are simulation results, a brief review of the literature, and some recommendations for practice.

Key words and phrases: Models, randomization, logistic regression, logit, average predicted probability.

1. INTRODUCTION

The logit model is often fitted to experimental data. As explained below, randomization does not justify the assumptions behind the model. Thus, the conventional estimator of log odds is difficult to interpret; an alternative will be suggested. Neyman’s setup is used to define parameters and prove results. (Grammatical niceties apart, the terms “logit model” and “logistic regression” are used interchangeably.)

After explaining the models and estimators, we present simulations to illustrate the findings. A brief review of the literature describes the history and current usage. Some practical recommendations are derived from the theory. Analytic proofs are sketched at the end of the paper.

2. NEYMAN

There is a study population with n subjects indexed by $i = 1, \dots, n$. Fix π_T with $0 < \pi_T < 1$. Choose $n\pi_T$ subjects at random and assign them to the treatment condition. The remaining $n\pi_C$ subjects are assigned to a control condition, where $\pi_C = 1 - \pi_T$. According to Neyman (1923), each subject has two responses: Y_i^T if assigned to treatment, and Y_i^C if assigned to control. The responses are 1 or 0, where 1 is “success” and 0 is “failure.” Responses are fixed, that is, not random.

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If i is assigned to treatment (T), then Y_i^T is observed. Conversely, if i is assigned to control (C), then Y_i^C is observed. Either one of the responses may be observed, but not both. Thus, responses are subject-level parameters. Even so, responses are estimable (see Section 9). Each subject has a covariate Z_i , unaffected by assignment; Z_i is observable. In this setup, the only stochastic element is the randomization: conditional on the assignment variable X_i , the observed response $Y_i = X_i Y_i^T + (1 - X_i) Y_i^C$ is deterministic.

Population-level ITT (intention-to-treat) parameters are defined by taking averages over all n subjects in the study population:

$$\begin{aligned} \alpha^T &= \frac{1}{n} \sum Y_i^T, \\ \alpha^C &= \frac{1}{n} \sum Y_i^C. \end{aligned} \tag{1}$$

For example, α^T is the fraction of successes if all subjects are assigned to T ; similarly for α^C . A parameter of considerable interest is the differential log odds of success,

$$\Delta = \log \frac{\alpha^T}{1 - \alpha^T} - \log \frac{\alpha^C}{1 - \alpha^C}. \tag{2}$$

The logit model is all about log odds (more on this below). The parameter Δ defined by (2) may therefore be what investigators think is estimated by running logistic regressions on experimental data, although that idea is seldom explicit.

The Intention-to-Treat Principle

The intention-to-treat principle, which goes back to Hill (1961, page 259), is to make comparisons based on treatment assigned rather than treatment received. Such comparisons take full advantage of the randomization, thereby avoiding biases due to self-selection. For example, the unbiased estimators for the parameters in (1) are the fraction of successes in the treatment group and the control group, respectively. Below, these will be called *ITT estimators*. ITT estimators measure the effect of assignment rather than treatment. With crossover, the distinction matters. For additional discussion, see Freedman (2006a).

3. THE LOGIT MODEL

To set up the logit model, we consider a study population of n subjects, indexed by $i = 1, \dots, n$. Each subject has three observable random variables: Y_i, X_i, Z_i . Here, Y_i is the response, which is 0 or 1. The primary interest is the “effect” of X_i on Y_i , and Z_i is a covariate.

For our purposes, the best way to formulate the model involves a latent (unobservable) random variable U_i for each subject. These are assumed to be independent across subjects, with a common *logistic distribution*: for $-\infty < u < \infty$,

$$(3) \quad P(U_i < u) = \exp(u) / [1 + \exp(u)],$$

where $\exp(u) = e^u$. The model assumes that X and Z are *exogenous*, that is, independent of U . More formally, $\{X_i, Z_i : i = 1, \dots, n\}$ is assumed to be independent of $\{U_i : i = 1, \dots, n\}$. Finally, the model assumes that $Y_i = 1$ if

$$\beta_1 + \beta_2 X_i + \beta_3 Z_i + U_i > 0;$$

else, $Y_i = 0$.

Given X and Z , it follows that responses are independent across subjects, the conditional probability that $Y_i = 1$ being $p(\beta, X_i, Z_i)$, where

$$(4) \quad p(\beta, x, z) = \frac{\exp(\beta_1 + \beta_2 x + \beta_3 z)}{1 + \exp(\beta_1 + \beta_2 x + \beta_3 z)}.$$

(To verify this, check first that $-U_i$ is distributed like $+U_i$.) The parameter vector $\beta = (\beta_1, \beta_2, \beta_3)$ is usually estimated by maximum likelihood. We denote the MLE by $\hat{\beta}$.

Interpreting the Coefficients in the Model

In the case of primary interest, X_i is 1 or 0. Consider the log odds λ_i^T of success when $X_i = 1$, as well as the log odds λ_i^C when $X_i = 0$. In view of (4),

$$\begin{aligned} \lambda_i^T &= \log \frac{p(\beta, 1, Z_i)}{1 - p(\beta, 1, Z_i)} \\ &= \beta_1 + \beta_2 + \beta_3 Z_i, \\ (5) \quad \lambda_i^C &= \log \frac{p(\beta, 0, Z_i)}{1 - p(\beta, 0, Z_i)} \\ &= \beta_1 + \beta_3 Z_i. \end{aligned}$$

In particular, $\lambda_i^T - \lambda_i^C = \beta_2$ for all i , whatever the value of Z_i may be. Thus, according to the model, $X_i = 1$ adds β_2 to the log odds of success.

Application to Experimental Data

To apply the model to experimental data, define $X_i = 1$ if i is assigned to T , while $X_i = 0$ if i assigned to C . Notice that the model not justified by randomization. Why would the logit specification be correct rather than the probit—or anything else? What justifies the choice of covariates? Why are they exogenous? If the model is wrong, what is $\hat{\beta}_2$ supposed to be estimating? The last rhetorical question may have an answer: the parameter Δ in (2) seems like a natural choice, as indicated above.

More technically, from Neyman’s perspective, given the assignment variables $\{X_i\}$, the responses are deterministic: $Y_i = Y_i^T$ if $X_i = 1$, while $Y_i = Y_i^C$ if $X_i = 0$. The logit model, on the other hand, views the responses $\{Y_i\}$ as random—with a specified distribution—given the assignment variables and covariates.

The contrast is therefore between two styles of inference.

- Randomization provides a known distribution for the assignment variables; statistical inferences are based on this distribution.
- Modeling assumes a distribution for the latent variables; statistical inferences are based on that assumption. Furthermore, model-based inferences are conditional on the assignment variables and covariates.

A similar contrast will be found in other areas too, including sample surveys. See Koch and Gillings (2005) for a review and pointers to the literature.

What if the Logit Model is Right?

Suppose the model is right, and there is a causal interpretation. We can intervene and set X_i to 1 without changing the Z 's or U 's, so $Y_i = 1$ if and only if $\beta_1 + \beta_2 + \beta_3 Z_i + U_i > 0$. Similarly, we can set X_i to 0 without changing anything else, and then $Y_i = 1$ if and only if $\beta_1 + \beta_3 Z_i + U_i > 0$. Notice that β_2 appears when X_i is set to 1, but disappears when X_i is set to 0.

On this basis, for each subject, whatever the value of Z_i may be, setting X_i to 1 rather than 0 adds β_2 to the log odds of success. If the model is right, β_2 is a very useful parameter, which is well estimated by the MLE provided n is large. For additional detail on causal modeling and estimation, see Freedman (2005).

Even if the model is right and n is large, β_2 differs from Δ in (2). For instance, α^T will be nearly equal to $\frac{1}{n} \sum_{i=1}^n p(\beta, 1, Z_i)$. So $\log \alpha^T - \log(1 - \alpha^T)$ will be nearly equal to

$$(6) \quad \log \left(\frac{1}{n} \sum_{i=1}^n p(\beta, 1, Z_i) \right) - \log \left(\frac{1}{n} \sum_{i=1}^n [1 - p(\beta, 1, Z_i)] \right).$$

Likewise, $\log \alpha^C - \log(1 - \alpha^C)$ will be nearly equal to

$$(7) \quad \log \left(\frac{1}{n} \sum_{i=1}^n p(\beta, 0, Z_i) \right) - \log \left(\frac{1}{n} \sum_{i=1}^n [1 - p(\beta, 0, Z_i)] \right).$$

Taking the log of an average, however, is quite different from taking the average of the logs. The former is relevant for Δ in (2), as shown by (6)–(7); the latter for computing

$$(8) \quad \frac{1}{n} \sum_{i=1}^n (\lambda_i^T - \lambda_i^C) = \beta_2,$$

where the log odds of success λ_i^T and λ_i^C were computed in (5).

The difference between averaging inside and outside the logs may be surprising at first, but in the end, that difference is why you should put confounders like Z into the equation—if you believe the model. Section 9 below gives further detail, and an inequality relating β_2 to Δ .

From Neyman to Logits

How could we get from Neyman to the logit model? To begin with, we would allow Y_i^T and Y_i^C to be 0–1 valued random variables; the Z_i can be random too. To define the parameters in (1) and (2), we would replace Y_i^T and Y_i^C by their expectations. None of this is problematic, and the Neyman model is now extremely general and flexible. Randomization makes the assignment variables $\{X_i\}$ independent of the potential responses Y_i^T, Y_i^C .

To get the logit model, however, we would need to specialize this setup considerably, assuming the existence of IID logistic random variables U_i , independent of the covariates Z_i , with

$$(9) \quad \begin{aligned} Y_i^T &= 1 && \text{if and only if} \\ &&& \beta_1 + \beta_2 + \beta_3 Z_i + U_i > 0, \\ Y_i^C &= 1 && \text{if and only if} \\ &&& \beta_1 + \beta_3 Z_i + U_i > 0. \end{aligned}$$

Besides (9), the restrictive assumptions are the following:

- (i) The U_i are independent of the Z_i .
- (ii) The U_i are independent across subjects i .
- (iii) The U_i have a common logistic distribution.

If you are willing to make these assumptions, what randomization contributes is a guarantee that the assignment variables $\{X_i\}$ are independent of the latent variables $\{U_i\}$. Randomization does not guarantee the existence of the U_i , or the truth of (9), or the validity of (i)–(iii).

4. A PLUG-IN ESTIMATOR FOR THE LOG ODDS

If a logit model is fitted to experimental data, average predicted probabilities are computed by plugging $\hat{\beta}$ into (4):

$$(10a) \quad \tilde{\alpha}^T = \frac{1}{n} \sum_{i=1}^n p(\hat{\beta}, 1, Z_i),$$

$$\tilde{\alpha}^C = \frac{1}{n} \sum_{i=1}^n p(\hat{\beta}, 0, Z_i).$$

(The tilde notation is needed; $\hat{\alpha}^T$ and $\hat{\alpha}^C$ will make their appearances momentarily.) Then the differential log odds in (2) can be estimated by plugging into the formula for Δ :

$$(10b) \quad \tilde{\Delta} = \log \frac{\tilde{\alpha}^T}{1 - \tilde{\alpha}^T} - \log \frac{\tilde{\alpha}^C}{1 - \tilde{\alpha}^C}.$$

As will be seen below, $\tilde{\Delta}$ is consistent.

The ITT (intention-to-treat) estimators are defined as follows:

$$(11a) \quad \hat{\alpha}^T = \frac{1}{n_T} \sum_{i \in T} Y_i, \quad \hat{\alpha}^C = \frac{1}{n_C} \sum_{i \in C} Y_i,$$

where $n_T = n\pi_T$ is the number of subjects in T and $n_C = n\pi_C$ is the number of subjects in C . Then

$$(11b) \quad \hat{\Delta} = \log \frac{\hat{\alpha}^T}{1 - \hat{\alpha}^T} - \log \frac{\hat{\alpha}^C}{1 - \hat{\alpha}^C}.$$

The ITT estimators are consistent too, with asymptotics discussed in Freedman (2008a, 2008b). The intuition: $\hat{\alpha}^T$ is the average success rate in the treatment group, and the sample average is a good estimator for the population average. The same reasoning applies to $\hat{\alpha}^C$.

5. SIMULATIONS

The simulations in this section are designed to show what happens when the logit model is fitted to experimental data. The data generating mechanism is not the logit, so the simulations illustrate the consequences of specification error. The stochastic element is the randomization, as in Section 2. (Some auxiliary randomness is introduced to construct the individual-level parameters, but that gets conditioned away.) Let $n = 100, 500, 1000, 5000$. For $i = 1, \dots, n$:

- let U_i, V_i be IID uniform random variables,
- let $Z_i = V_i$,
- let $Y_i^C = 1$ if $U_i > 1/2$, else $Y_i^C = 0$,
- let $Y_i^T = 1$ if $U_i + V_i > 3/4$, else $Y_i^T = 0$.

Suppose n is very large. The mean response in the control condition is around $P(U_i > 1/2) = 1/2$, so the odds of success in the control condition are around 1. (The qualifiers are needed because the U_i are chosen at random.) The mean response in the treatment condition is around 23/32, because

$$P(U_i + V_i < 3/4) = (1/2) \times (3/4)^2 = 9/32.$$

So the odds of success in the treatment condition are around $(23/32)/(9/32)$. The parameter Δ in (2) will therefore be around

$$\log \frac{23/32}{9/32} - \log 1 = \log \frac{23}{9} = 0.938.$$

Even for moderately large n , non-linearity in (2) is an issue, and the approximation given for Δ is unsatisfactory.

The construction produces individual-level variation: a majority of subjects are unaffected by treatment,

TABLE 1

Simulations for $n = 100, 500, 1000, 5000$. Twenty-five percent of the subjects are assigned at random to C , the rest to T . Averages and SDs are shown for the MLE $\hat{\beta}$ and the plug-in estimator $\tilde{\Delta}$, as well as the true value of the differential log odds Δ defined in (2). There are 1,000 simulated experiments for each n

n	$\hat{\beta}_1$	$\hat{\beta}_2$	$\hat{\beta}_3$	Plug-in	Truth
100	-0.699	1.344	2.327	1.248	1.245
	0.457	0.540	0.621	0.499	
500	-1.750	1.263	3.318	1.053	1.053
	0.214	0.234	0.227	0.194	
1000	-1.568	1.046	3.173	0.885	0.883
	0.155	0.169	0.154	0.142	
5000	-1.676	1.134	3.333	0.937	0.939
	0.071	0.076	0.072	0.062	

about 1/4 are helped, about 1/32 are harmed. The covariate is reasonably informative about the effect of treatment—if Z_i is big, treatment is likely to help.

Having constructed Z_i, Y_i^C and Y_i^T for $i = 1, \dots, n$, we freeze them, and simulate 1000 randomized controlled experiments, where 25% of the subjects are assigned to C and 75% to T . We fit a logit model to the data generated by each experiment, computing the MLE $\hat{\beta}$ and the plug-in estimator $\tilde{\Delta}$ defined by (10b). The average of the 1000 $\hat{\beta}$'s and $\tilde{\Delta}$'s is shown in Table 1, along with the true value of the differential log odds, namely, Δ in (2). We distinguish between the standard deviation (SD) and the standard error (SE). Below each average, the table shows the corresponding SD.

For example, with $n = 100$, the average of the 1000 $\hat{\beta}_2$'s is 1.344; the SD is 0.540; the Monte Carlo SE in the average is therefore $0.540/\sqrt{1000} = 0.017$. The average of the 1000 plug-in estimates is 1.248, and the true Δ is 1.245. When $n = 5000$, the bias in $\hat{\beta}_2$ as an estimator of Δ is $1.134 - 0.939 = 0.195$, with a Monte Carlo SE of $0.076/\sqrt{1000} = 0.002$. There is a confusion to avoid: n is the number of subjects in the study population, varying from 100 to 5000, but the number of simulated experiments is fixed at 1000. (The *Monte Carlo SE* measures the impact of randomness in the simulation, which is based on a sample of “only” 1000 observations.)

The plug-in estimator is essentially unbiased and less variable than $\hat{\beta}_2$. The true value of Δ changes from one n to the next, since values of Y_i^C, Y_i^T are generated by Monte Carlo for each n . Even with $n = 5000$, the true value of Δ would change from one run to another, the SD across runs being about 0.03 (not shown in the table).

Parameter choices—for instance, the joint distribution of (U_i, V_i) —were somewhat arbitrary. Surprisingly, bias depends on the fraction of subjects assigned to T . On the other hand, changing the cutpoints used to define Y_i^C and Y_i^T from 1/2 and 3/4 to 0.95 and 1.5 makes little difference to the performance of $\hat{\beta}_2$ and the plug-in estimator. In these examples, the plug-in estimator and the ITT estimators are essentially unbiased; the latter has slightly smaller variance.

The bias in $\hat{\beta}_2$ depends very much on the covariate. For instance, if the covariate is $U_i + V_i$ rather than V_i , then $\hat{\beta}_2$ hovers around 3. Truth remains in the vicinity of 1, so the bias in $\hat{\beta}_2$ is huge. The plug-in and ITT estimators remain essentially unbiased, with variances much smaller than $\hat{\beta}_2$; the ITT estimator has higher variance than the plug-in estimator (data not shown for variations on the basic setup, or ITT estimators).

The Monte Carlo results suggest the following:

- (i) As n gets large, the MLE $\hat{\beta}$ stabilizes.
- (ii) The plug-in estimator $\tilde{\Delta}$ is a good estimator of the differential log odds Δ .
- (iii) $\hat{\beta}_2$ tends to over-estimate $\Delta > 0$.

These points will be verified analytically below.

6. EXTENSIONS AND IMPLICATIONS

Suppose the differential log odds of success is the parameter to be estimated. Then $\hat{\beta}_2$ is generally the wrong estimator to use—whether the logit model is right or the logit model is wrong (Section 9 has a mathematical proof). It is better to use the plug-in estimator (10) or the ITT estimator (11). These estimators are nearly unbiased, and in many examples have smaller variances too.

Although details remain to be checked, the convergence arguments in Section 8 seem to extend to probits, the parameter corresponding to (2) being

$$\Phi^{-1}(\alpha^T) - \Phi^{-1}(\alpha^C),$$

where Φ is the standard normal distribution function. On the other hand, with the probit, the plug-in estimators are unlikely to be consistent, since the analogs of the likelihood equations (16)–(18) below involve weighted averages rather than simple averages.

In simulation studies (not reported here), the probit behaves very much like the logit, with the usual difference in scale: probit coefficients are about 5/8 of their logit counterparts (Amemiya, 1981, page 1487). Numerical calculations also confirm inconsistency of the plug-in estimators, although the asymptotic bias is small.

According to the logit and probit models, if treatment improves the chances of success, it does so for all subjects. In reality, of course, treatment may help some subgroups and hurt others. Subgroup analysis can therefore be a useful check on the models. Consistency of the plug-in estimators—as defined here—does not preclude subgroup effects.

Logit models, probit models, and their ilk are not justified by randomization. This has implications for practice. Rates and averages for the treatment and control groups should be compared before the modeling starts. If the models change the substantive results, that raises questions that need to be addressed.

There may be an objection that models take advantage of additional information. The objection has some merit *if* the models are right or nearly right. On the other hand, if the models cannot be validated, conclusions drawn from them must be shaky. “Cross-tabulation before regression” is a slogan to be considered.

7. LITERATURE REVIEW

Logit and probit models are often used to analyze experimental data. See Pate and Hamilton (1992), Gilens (2001), Hu (2003), Duch and Palmer (2004), Frey and Meier (2004), Gertler (2004). The plug-in estimator discussed here is similar to the “average treatment effect” sometimes reported in the literature; see, for example, Evans and Schwab (1995). For additional discussion, see Lane and Nelder (1982), Brant (1996).

Lim (1999) conjectured that plug-in estimators based on the logit model would be consistent, with an informal argument based on the likelihood equation. He also conjectured inconsistency for the probit. Middleton (2007) discusses inconsistent logit estimators.

The logistic distribution may first have been used to model population growth. See Verhulst (1845) and Yule (1925). Later, the distribution was used to model dose-response in bioassays (Berkson, 1944). An early biomedical application to causal inference is Truett, Cornfield, and Kannel (1967). The history is considered further in Freedman (2005). The present paper extends previous results on linear regression (Freedman, 2008a, 2008b).

Statistical models for causation go back to Jerzy Neyman’s work on agricultural experiments in the early part of the 20th century. The key paper, Neyman (1923), was in Polish. There was an extended discussion by Scheffé (1956), and an English translation by Dabrowska and Speed (1990). The model was covered

in elementary textbooks in the 1960s; see, for instance, Hodges and Lehmann (1964, Section 9.4). The setup is often called “Rubin’s model,” due in part to Holland (1986); that mistakes the history.

Neyman, Kolodziejczyk, and Iwaszkiewicz (1935) develop models with subject-specific random effects that depend on assignment, the objective being to estimate average expected values under various circumstances. This is discussed in Section 4 of Scheffé (1956).

Heckman (2000) explains the role of potential outcomes in econometrics. In epidemiology, a good source is Robins (1999). Rosenbaum (2002) proposes using models and permutation tests as devices for hypothesis-testing. This avoids difficulties outlined here: (i) if treatment has no effect, then $Y_i^T = Y_i^C = Y_i$ for all i , and (ii) randomization makes all permutations of i equally likely—which is just what permutation tests need.

Rosenblum and van der Laan (2008) suggest that, at least for purposes of hypothesis testing, robust SEs will fix problems created by specification error. Such optimism is unwarranted. Under the alternative hypothesis, the robust SE is unsatisfactory because it ignores bias (Freedman, 2006b).

Under the null hypothesis, the robust SE may be asymptotically correct, but using it can reduce power (Freedman, 2008a, 2008b). In any event, if the null hypothesis is to be tested using model-based adjustments, exact P -values can be computed by permutation methods, as suggested by Rosenbaum (2002).

Models are often deployed to infer causation from association. For a discussion from various perspectives, see Berk (2004), Brady and Collier (2004), and Freedman (2005). The last summarizes a cross-section of the literature on this topic (pages 192–200).

Consider a logit model like the one in Section 3. Omitting the covariate Z from the equation is called *marginalizing* over Z . The model is *collapsible* if the marginal model is again logit with the same β_2 . In other words, given the X ’s, the Y ’s are conditionally independent, and

$$P(Y_i = 1|X_i) = \frac{\exp(\beta_1 + \beta_2 X_i)}{1 + \exp(\beta_1 + \beta_2 X_i)}.$$

Guo and Geng (1995) give conditions for collapsibility; also see Ducharme and Lepage (1986). Gail (1986, 1988) discusses collapsing when a design is balanced. Robinson and Jewell (1991) show that collapsing will usually decrease variance: logit models differ from linear models. Aris et al. (2000) review the literature and consider modeling strategies to compensate for non-collapsibility.

8. SKETCH OF PROOFS

We are fitting the logit model, which is incorrect, to data from an experiment. As before, let X_i be the assignment variable, so $X_i = 1$ if $i \in T$ and $X_i = 0$ if $i \in C$. Let Y_i be the observed response, so $Y_i = X_i Y_i^T + (1 - X_i) Y_i^C$. Let $L_n(\beta)$ be the “log-likelihood function” to be maximized. The quote marks are there because the model is wrong; L_n is therefore only a pseudo-log-likelihood function. Abbreviate $p_i(\beta)$ for $p(\beta, X_i, Z_i)$ in (4). The formula for $L_n(\beta)$ is this:

$$(12a) \quad L_n(\beta) = \sum_{i=1}^n T_i,$$

where

$$(12b) \quad \begin{aligned} T_i &= \log[1 - p_i(\beta)] \\ &\quad + (\beta_1 + \beta_2 X_i + \beta_3 Z_i) Y_i. \end{aligned}$$

(The T is for term, not treatment.) It takes a moment to verify (12), starting from the equation

$$(13) \quad T_i = Y_i \log(p_i) + (1 - Y_i) \log(1 - p_i).$$

Each T_i is negative. The function $\beta \rightarrow L_n(\beta)$ is strictly concave, as one sees by proving that L_n'' is a negative definite matrix. Consequently, there is a unique maximum at the MLE $\hat{\beta}_n$. We write $\hat{\beta}_n$ to show dependence on the size n of the study population, although that creates a conflict in the notation. If pressed, we could write $\hat{\beta}_{n,j}$ for the j th component of the MLE.

The i th row of the “design matrix” is $(1, X_i, Z_i)$. Tacitly, we are assuming this matrix is nonsingular. For large n , the assumption will follow from regularity conditions to be imposed. The concavity of L_n is well known. See, for instance, pages 122–123 in Freedman (2005) or page 273 in Amemiya (1985). Pratt (1981) discusses the history and proves a more general result.

For reference, we record one variation on these ideas. Let M be an $n \times p$ matrix of rank p ; write M_i for the i th row of M . Let y be an $n \times 1$ vector of 0s and 1s. Let β be a $p \times 1$ vector. Let $w_i > 0$ for $i = 1, \dots, n$. Consider M and y as fixed, β as variable. Define $L(\beta)$ as

$$\sum_{i=1}^n w_i \{-\log[1 + \exp(M_i \cdot \beta)] + (M_i \cdot \beta) y_i\}.$$

PROPOSITION 1. *The function $\beta \rightarrow L(\beta)$ is strictly concave.*

One objective in the rest of this section is showing that

$$(14) \quad \beta_n \text{ converges to a limit } \beta_\infty \text{ as } n \rightarrow \infty.$$

A second objective is showing that

(15) the plug-in estimator $\tilde{\Delta}$ is consistent.

The argument actually shows a little more. The plug-in estimator $\tilde{\alpha}^T$, the ITT estimator $\hat{\alpha}^T$, and the parameter α^T become indistinguishable as the size n of the study population grows; likewise for $\tilde{\alpha}^C$, $\hat{\alpha}^C$ and α^C .

The ITT estimators $\hat{\alpha}^T$, $\hat{\alpha}^C$ were defined in (11). Recall too that $n_T = n\pi_T$ and $n_C = n\pi_C$ are the numbers of subjects in T and C respectively. The statement of Lemma 1 involves the empirical distribution of Z_i for $i \in T$, which assigns mass $1/n_T$ to Z_i for each $i \in T$. Similarly, the empirical distribution of Z_i for $i \in C$ assigns mass $1/n_C$ to Z_i for each $i \in C$.

To prove Lemma 1, we need the likelihood equation $L'_n(\beta) = 0$. This vector equation unpacks to three scalar equations in three unknowns, the components of β that make up $\hat{\beta}_n$:

$$(16) \quad \frac{1}{n_T} \sum_{i \in T} p(\hat{\beta}_n, 1, Z_i) = \frac{1}{n_T} \sum_{i \in T} Y_i,$$

$$(17) \quad \frac{1}{n_C} \sum_{i \in C} p(\hat{\beta}_n, 0, Z_i) = \frac{1}{n_C} \sum_{i \in C} Y_i,$$

$$(18) \quad \frac{1}{n} \sum_{i=1}^n p(\hat{\beta}_n, X_i, Z_i) Z_i = \frac{1}{n} \sum_{i=1}^n Y_i Z_i.$$

This follows from (12)–(13) after differentiating with respect to β_1 , β_2 , and β_3 —and then doing a bit of algebra.

LEMMA 1. *If the empirical distribution of Z_i for $i \in T$ matches the empirical distribution for $i \in C$ (the first balance condition), then the plug-in estimators $\tilde{\alpha}^T$, $\tilde{\alpha}^C$ match the ITT estimators. More explicitly,*

$$\frac{1}{n} \sum_{i=1}^n p(\hat{\beta}_n, 1, Z_i) = \frac{1}{n_T} \sum_{i \in T} Y_i,$$

$$\frac{1}{n} \sum_{i=1}^n p(\hat{\beta}_n, 0, Z_i) = \frac{1}{n_C} \sum_{i \in C} Y_i.$$

PROOF. The plug-in estimators $\tilde{\alpha}^T$, $\tilde{\alpha}^C$ were defined in (10); the ITT estimators $\hat{\alpha}^T$, $\hat{\alpha}^C$, in (11). We begin with $\tilde{\alpha}^T$. By (16),

$$\frac{1}{n_T} \sum_{i \in T} p(\hat{\beta}_n, 1, Z_i) = \frac{1}{n_T} \sum_{i \in T} Y_i = \hat{\alpha}^T.$$

By the balance condition,

$$\frac{1}{n_C} \sum_{i \in C} p(\hat{\beta}_n, 1, Z_i) = \frac{1}{n_T} \sum_{i \in T} p(\hat{\beta}_n, 1, Z_i)$$

equals $\hat{\alpha}^T$ too. Finally, the average of $p(\hat{\beta}_n, 1, Z_i)$ over all i is a mixture of the averages over T and C . So $\tilde{\alpha}^T = \hat{\alpha}^T$ as required. The same argument works for $\tilde{\alpha}^C$, using (17). \square

For the next lemma, recall α^T , α^C from (1). The easy proof is omitted, being very similar to the proof of the previous result.

LEMMA 2. *Suppose the empirical distribution of the pairs (Y_i^T, Y_i^C) for $i \in T$ matches the empirical distribution for $i \in C$ (the second balance condition). Then $\hat{\alpha}^T = \alpha^T$ and $\hat{\alpha}^C = \alpha^C$.*

LEMMA 3. *Let x be any real number. Then*

$$e^x - \frac{1}{2}e^{2x} < \log(1 + e^x) < e^x,$$

$$x + e^{-x} - \frac{1}{2}e^{-2x} < \log(1 + e^x) < x + e^{-x}.$$

The first bound is useful when x is large and negative; the second, when x is large and positive. To get the second bound from the first, write $1 + e^x = e^x(1 + e^{-x})$, then replace x by $-x$. The first bound will look more familiar on substituting $y = e^x$. The proof is omitted, being “just” calculus.

For the next result, let G be an open, bounded, convex subset of Euclidean space. Let f_n be a strictly concave function on G , converging uniformly to f_∞ , which is also strictly concave. Let f_n take its maximum at x_n , while f_∞ takes its maximum at $x_\infty \in G$. Although the lemma is well known, a proof may be helpful. We write $G \setminus H$ for the set of points that are in G but not in H .

LEMMA 4. $x_n \rightarrow x_\infty$ and $f_n(x_n) \rightarrow f_\infty(x_\infty)$.

PROOF. Choose a small neighborhood H of $x_\infty = \arg \max f_\infty$. There is a small positive δ with $f_\infty(x) < f_\infty(x_\infty) - \delta$ for $x \in G \setminus H$. For all sufficiently large n , we have $|f_n - f_\infty| < \delta/3$. In particular, $f_n(x_\infty) > f_\infty(x_\infty) - \delta/3$. On the other hand, if $x \in G \setminus H$, then

$$f_n(x) < f_\infty(x) + \delta/3 < f_\infty(x_\infty) - 2\delta/3.$$

Thus, $\arg \max f_n \in H$. Furthermore, $f_n(x_n) \geq f_n(x_\infty) > f_\infty(x_\infty) - \delta/3$. In the other direction, $f_\infty(x_\infty) \geq f_\infty(x_n) > f_n(x_n) - \delta/3$. So

$$|\max f_n - \max f_\infty| < \delta/3,$$

which completes the proof. \square

For the final lemma, consider a population consisting of n objects. Suppose r are red, and $r/n \rightarrow \rho$ with $0 < \rho < 1$. (The remaining $n - r$ objects are colored black.) Now choose m out of the n objects at random without

replacement, where $m/n \rightarrow \lambda$ with $0 < \lambda < 1$. Let X_m be the number of red objects that are chosen. So X_m is hypergeometric. The lemma puts no conditions on the joint distribution of the $\{X_m\}$. Only the marginals are relevant.

LEMMA 5. $X_m/n \rightarrow \lambda\rho$ almost surely as $n \rightarrow \infty$.

PROOF. Of course, $E(X_m) = rm/n$. The lemma can be proved by using Chebychev's inequality, after showing that

$$E\left[\left(X_m - r\frac{m}{n}\right)^4\right] = O(n^2).$$

Tedious algebra can be reduced by appealing to Theorem 4 in Hoeffding (1963). In more detail, let W_i be independent 0–1 variables with $P(W_i = 1) = r/n$. Thus, $\sum_{i=1}^m W_i$ is the number of reds in m draws with replacement, while X_m is the number of reds in m draws without replacement. According to Hoeffding's theorem, X_m is more concentrated around the common expected value. In particular,

$$E\left\{\left(X_m - r\frac{m}{n}\right)^4\right\} < E\left\{\left[\sum_{i=1}^m\left(W_i - \frac{r}{n}\right)\right]^4\right\}.$$

Expanding $[\sum_{i=1}^m(W_i - \frac{r}{n})]^4$ yields m terms of the form $(W_i - \frac{r}{n})^4$. Each of these terms is bounded above by 1. Next consider terms like $(W_i - \frac{r}{n})^2(W_j - \frac{r}{n})^2$ with $i \neq j$. The number of such terms is of order m^2 , and each term is bounded above by 1. All remaining terms have expectation 0. Thus, $E[(X_m - r\frac{m}{n})^4]$ is of order $m^2 < n^2$. \square

NOTE. There are m^4 terms in $(a_1 + \dots + a_m)^4 = \sum_{ijkl} a_i a_j a_k a_l$. By combinatorial arguments:

- (i) m terms are like a_i^4 , with one index only.
- (ii) $3m(m-1)$ are like $a_i^2 a_j^2$, with two different indices.
- (iii) $4m(m-1)$ are like $a_i^3 a_j$, with two different indices.
- (iv) $6m(m-1)(m-2)$ are like $a_i^2 a_j a_k$, with three different indices.
- (v) $m(m-1)(m-2)(m-3)$ are like $a_i a_j a_k a_l$, with four different indices.

The counts can also be derived from the “multinomial theorem,” which expands $(a_1 + \dots + a_m)^N$. For an early—and very clear—textbook exposition, see Chrystal (1889, pages 14–15). A little care is needed, since our counts do not restrict the order of the indices: $i < j$ and $i > j$ are both allowed. By contrast,

in the usual statements of the multinomial theorem, indices are ordered ($i < j$). German scholarship traces the theorem (“der polynomische Lehrsatz”) back to correspondence between Leibniz and Johann Bernoulli in 1695; see, for instance, Tauber (1963), Netto (1927, page 58), and Tropicke (1903, page 332). On the other hand, de Moivre (1697) surely deserves some credit.

We return now to our main objectives. In outline, we must show that $L_n(\beta)/n$ converges to a limit $L_\infty(\beta)$, uniformly over β in any bounded set; this will follow from Lemma 5. The limiting $L_\infty(\beta)$ is a strictly concave function of β , with a unique maximum at β_∞ : see Proposition 1. Furthermore, $\hat{\beta}_n \rightarrow \beta_\infty$ by Lemma 4. In principle, randomization ensures that the balance conditions are nearly satisfied, so the plug-in estimator is consistent by Lemmas 1–2. A rigorous argument gets somewhat intricate; one difficulty is showing that remote β 's can be ignored, and Lemma 3 helps in this respect.

Some regularity conditions are needed. Technicalities will be minimized if we assume that Z_i takes only a finite number of values; notational overhead is reduced even further if $Z_i = 0, 1$, or 2 . There are now $3 \times 2 \times 2 = 12$ possible values for the triples Z_i, Y_i^C, Y_i^T . We say that subject i is of type zct provided

$$Z_i = z, \quad Y_i^C = c, \quad Y_i^T = t.$$

Let $\theta_{z,c,t}$ be the fraction of subjects that are of type zct ; the number of these subjects is $n\theta_{z,c,t}$.

The θ 's are population-level parameters. They are not random. They sum to 1. We assume the θ 's are all positive. Recall that π_T is the fraction of subjects assigned to T . This is fixed (not random), and $0 < \pi_T < 1$. The fraction assigned to C is $\pi_C = 1 - \pi_T$. In principle, π_T, π_C , and the $\theta_{z,c,t}$ depend on n . As n increases, we assume these quantities have respective limits λ_T, λ_C and $\lambda_{z,c,t}$, all positive. Since z takes only finitely many values, $\sum_{z,c,t} \lambda_{z,c,t} = 1$.

When n is large, within type zct , the fraction of subjects assigned to T is random, but essentially λ_T : such subjects necessarily have response $Y_i = t$. Likewise, the fraction assigned to C is random, but essentially λ_C : such subjects necessarily have response $Y_i = c$. In the limit, the Z 's are exactly balanced between T and C within each type of subject. That is the essence of the argument; details follow.

Within type zct , let $n_{z,c,t}^T$ and $n_{z,c,t}^C$ be the number of subjects assigned to T and C , respectively. So

$$n_{z,c,t}^T + n_{z,c,t}^C = n\theta_{z,c,t}.$$

The variables $n_{z,c,t}^T$ are hypergeometric. They are unobservable. This is because type is unobservable: Y_i^C and Y_i^T are not simultaneously observable.

To analyze the log-likelihood function $L_n(\beta)$, recall that $Y_i = X_i Y_i^T + (1 - X_i) Y_i^C$ is the observed response. Let $n_{z,x,y}$ be the number of i with $Z_i = z$, $X_i = x$, $Y_i = y$; here $z = 0, 1$, or 2 , $x = 0$ or 1 , and $y = 0$ or 1 . The $n_{z,x,y}$ are observable because Y_i is observable. They are random because X_i is random. Also let $n_{z,x} = n_{z,x,0} + n_{z,x,1}$, which is the number of subjects i with $Z_i = z$ and $X_i = x$. Now $L_n(\beta)/n$ in (12) is the sum

$$(19a) \quad \sum_{z,x} T_{z,x},$$

where

$$(19b) \quad T_{z,x} = -\frac{n_{z,x}}{n} \log[1 + \exp(\beta_1 + \beta_2 x + \beta_3 z)] + \frac{n_{z,x,1}}{n} (\beta_1 + \beta_2 x + \beta_3 z).$$

(Again, T is for “term,” not “treatment.”) This can be checked by grouping the terms T_i in (12) according to the possible values of (Z_i, X_i, Y_i) . There are six terms $T_{z,x}$ in (19), corresponding to $z = 0, 1$, or 2 and $x = 0$ or 1 .

We claim

$$(20) \quad \begin{aligned} n_{z,x,y} &= n_{z,0,y}^T + n_{z,1,y}^T & \text{if } x = 1, \\ &= n_{z,y,0}^C + n_{z,y,1}^C & \text{if } x = 0. \end{aligned}$$

The trick is seeing through the notation. For instance, take $x = 1$. By definition, $n_{z,1,y}$ is the number of i with $Z_i = z$, $X_i = 1$, $Y_i = y$. The i 's with $X_i = 1$ correspond to subjects in the treatment group, so $Y_i = Y_i^T$. Thus, $n_{z,1,y}$ is the number of i with $Z_i = z$, $X_i = 1$, $Y_i^T = y$. Also by definition, $n_{z,c,y}^T$ is the number of subjects with $Z_i = z$, $X_i = 1$, $Y_i^C = c$, $Y_i^T = y$. Now add the numbers for $c = 0, 1$: how these subjects would have responded to the control regime is at this point irrelevant. A similar argument works if $x = 0$, completing the discussion of (20).

Recall that $\theta_{z,c,y} \rightarrow \lambda_{z,c,y}$ as $n \rightarrow \infty$. Let

$$\theta_z = \sum_{c,y} \theta_{z,c,y} \quad \text{and} \quad \lambda_z = \sum_{c,y} \lambda_{z,c,y}.$$

Thus, θ_z is the fraction of subjects with $Z_i = z$, and $\theta_z \rightarrow \lambda_z$ as $n \rightarrow \infty$.

As $n \rightarrow \infty$, we claim that

$$(21) \quad n_{z,1,y}/n \rightarrow \lambda_T (\lambda_{z,0,y} + \lambda_{z,1,y}),$$

$$(22) \quad n_{z,1}/n \rightarrow \lambda_T \lambda_z,$$

$$(23) \quad n_{z,0,y}/n \rightarrow \lambda_C (\lambda_{z,y,0} + \lambda_{z,y,1}),$$

$$(24) \quad n_{z,0}/n \rightarrow \lambda_C \lambda_z,$$

where, for instance, λ_T is the limit of π_T as $n \rightarrow \infty$. More specifically, there a set \mathcal{N} of probability 0, and (21)–(24) hold true outside of \mathcal{N} . Indeed, (21) follows from (20) and Lemma 5. Then (22) follows from (21) by addition over $y = 0, 1$. The last two lines are similar to the first two.

A little more detail on (21) may be helpful. What is the connection with Lemma 5? Consider $n_{z,0,y}^T$, which is the number of subjects of type $z0y$ that are assigned to T . The “reds” are subjects of type $z0y$, so the fraction of reds in the population converges to $\lambda_{z,0,y}$, by assumption. We are drawing m times at random without replacement from the population to get the treatment group, and $m/n \rightarrow \lambda_T$, also by assumption. Now X_m is the number of reds in the sample, that is, the number of subjects of type $z0y$ assigned to treatment. The lemma tells us that $X_m \rightarrow \lambda_T \lambda_{z,0,y}$ almost surely. The same argument works for $n_{z,1,y}^T$. Add to get (21).

Next, fix a positive, finite, real number B . Consider the open, bounded, convex polyhedron G_B defined by the six inequalities

$$(25) \quad |\beta_1 + \beta_2 x + \beta_3 z| < B$$

for $x = 0, 1$ and $z = 0, 1, 2$. As $n \rightarrow \infty$, we claim that $L_n(\beta)/n \rightarrow L_\infty(\beta)$ uniformly over $\beta \in G_B$, where

$$(26a) \quad L_\infty(\beta) = \lambda_T \Lambda_T + \lambda_C \Lambda_C,$$

$$(26b) \quad \begin{aligned} \Lambda_T &= \sum_z (-\lambda_z \log[1 + \exp(\phi_T(z))]) \\ &\quad + (\lambda_{z,0,1} + \lambda_{z,1,1}) \phi_T(z), \end{aligned}$$

$$(26c) \quad \begin{aligned} \Lambda_C &= \sum_z (-\lambda_z \log[1 + \exp(\phi_C(z))]) \\ &\quad + (\lambda_{z,1,0} + \lambda_{z,1,1}) \phi_C(z), \end{aligned}$$

$$(26d) \quad \phi_T(z) = \beta_1 + \beta_2 + \beta_3 z,$$

$$\phi_C(z) = \beta_1 + \beta_3 z.$$

(Recall that λ_T was the limit of π_T as $n \rightarrow \infty$, and likewise for λ_C .) This follows from (21)–(24), on splitting the sum in (19) into two sums, one with terms $z1$ and the other with terms $z0$. The $z1$ terms give us $\lambda_T \Lambda_T$, and the $z0$ terms give us $\lambda_C \Lambda_C$. The conclusion holds outside the null set \mathcal{N} defined for (21)–(24).

It may be useful to express the limiting distribution of $\{Z, X, Y\}$ in terms of λ_T, λ_C and $\lambda_{z,c,t}$, the latter being the limiting fraction of subjects of type zct . See Table 2. For example, what fraction of subjects have $Z = z, X = 1, Y = 1$ in the limit? The answer is the first row, second column of the table. The other entries can be read in a similar way.

TABLE 2
Asymptotic distribution of $\{Z, X, Y\}$
expressed in terms of λ_T, λ_C and $\lambda_{z,c,t}$

Value	Weight
$z11$	$\lambda_T(\lambda_{z,0,1} + \lambda_{z,1,1})$
$z10$	$\lambda_T(\lambda_{z,0,0} + \lambda_{z,1,0})$
$z01$	$\lambda_C(\lambda_{z,1,0} + \lambda_{z,1,1})$
$z00$	$\lambda_C(\lambda_{z,0,0} + \lambda_{z,0,1})$

The function $\beta \rightarrow L_\infty(\beta)$ is strictly concave, by Proposition 1 with $n = 12$ and $p = 3$. The rows of $(M y)$ run through all 12 combinations of $1 z x y$ with $z = 1, 2, 3$, and $x = 0, 1$, and $y = 0, 1$. The weights are shown in Table 2.

Let β_∞ be the β that maximizes $L_\infty(\beta)$. Choose B in (25) so large that $\beta_\infty \in G_B$. Lemma 4 shows that $\max_{\beta \in G_B} L_n(\beta)/n$ is close to $L_\infty(\beta_\infty)$ for all large n . Outside G_B —if B is large enough— $L_n(\beta)/n$ is too small to matter; additional detail is given below. Thus, $\hat{\beta}_n \in G_B$ for all large n , and converges to β_∞ .

This completes the argument for (14) and we turn to proving (15)—the consistency of the plug-in estimators defined by (10). Recall that θ_z is the fraction of i 's with $Z_i = z$; and $\theta_z \rightarrow \lambda_z$ as $n \rightarrow \infty$. Now

$$\begin{aligned} \tilde{\alpha}^T &= \frac{1}{n} \sum_{i=1}^n p(\hat{\beta}_n, 1, Z_i) \\ &= \sum_z \theta_z p(\hat{\beta}_n, 1, z) \\ &\rightarrow \sum_z \lambda_z p(\beta_\infty, 1, z), \end{aligned}$$

where the function $p(\beta, x, z)$ was defined in (4). Remember, z takes only finitely many values! A similar argument shows that $\tilde{\alpha}^C \rightarrow \sum_z \lambda_z p(\beta_\infty, 0, z)$.

The limiting distribution for $\{Z_i, Y_i^C, Y_i^T\}$ is defined by the $\lambda_{z,c,t}$, where $\lambda_{z,c,t}$ is the limiting fraction of subjects of type zct ; recall that $\lambda_z = \sum_{c,t} \lambda_{z,c,t}$. We claim

$$(27) \quad \sum_z \lambda_z p(\beta_\infty, 1, z) = \sum_{z,c} \lambda_{z,c,1},$$

$$(28) \quad \sum_z \lambda_z p(\beta_\infty, 0, z) = \sum_{z,t} \lambda_{z,1,t}.$$

Indeed, (22) and (24) show that in the limit, the Z_i are exactly balanced between T and C . Likewise, (21) and (23) show that in the limit, the pairs Y_i^T, Y_i^C are exactly balanced between T and C . Apply Lemmas 1–2. The left-hand side of (27) is the plug-in estimator for

the limiting α^T . The right-hand side is the ITT estimator, as well as truth. The three values coincide by the lemmas. The argument for (28) is the same, completing the discussion of (27)–(28).

The right-hand side of (27) can be recognized as the limit of $\frac{1}{n} \sum_{i=1}^n Y_i^T = \sum_{z,c} \theta_{z,c,1}$; likewise, the right-hand side of (28) is the limit of $\frac{1}{n} \sum_{i=1}^n Y_i^C$. This completes the proof of (15). In effect, the argument parlays Fisher consistency into almost-sure consistency, the exceptional null set being the \mathcal{N} where (21)–(24) fail.

Our results give an indirect characterization of $\lim \beta_n$ as the β at which the limiting log-likelihood function (26) takes on its maximum. Furthermore, asymptotic normality of $\{n_{z,c,t}^T\}$ entails asymptotic normality of $\hat{\beta}_n$ and the plug-in estimators, but that is a topic for another day.

Additional Detail on Boundedness

Consider a $z1$ term in (19). We are going to show that for B large, this term is too small to matter. Fix a small positive ϵ . By (22), for all large n ,

$$n_{z,1}/n > (1 - \epsilon)\lambda_T\lambda_z;$$

by (21),

$$n_{z,1,1}/n < (1 + \epsilon)\lambda_T(\lambda_{z,0,1} + \lambda_{z,1,1}).$$

Let $z' = \beta_1 + \beta_2 + \beta_3 z \geq B > 0$. By Lemma 3,

$$\log[1 + \exp(z')] > z' + \exp(-z') - \frac{1}{2} \exp(-2z') > z'$$

because $z' \geq B > 0$. Our $z1$ term is therefore bounded above for all large n by

$$[-(1 - \epsilon)\lambda_z + (1 + \epsilon)(\lambda_{z,0,1} + \lambda_{z,1,1})]\lambda_T z'.$$

The largeness needed in n depends on ϵ not B .

We can choose $\epsilon > 0$ so small that

$$(1 + \epsilon)(\lambda_{z,0,1} + \lambda_{z,1,1}) < (1 - 2\epsilon)\lambda_z,$$

because $\lambda_{z,0,1} + \lambda_{z,1,1} < \lambda_z$. Our $z1$ term is therefore bounded above by $-\epsilon\lambda_T\lambda_z B$. For B large enough, this term is so negative as to be irrelevant. The argument works because all $\lambda_{z,c,t}$ are assumed positive, and there are only finitely many of them. A similar argument works for $z' = \beta_1 + \beta_2 + \beta_3 z \leq -B$, and for terms $z0$ in (19). These arguments go through outside the null set \mathcal{N} defined for (21)–(24).

Summing up

It may be useful to summarize the results so far. The parameter α^T is defined in terms of the study population, as the fraction of successes that would be obtained if all members of the population were assigned to treatment; likewise for α^C . See (1). The differential log odds Δ of success is defined by (2). There is a covariate taking a finite number of values. A fraction of the subjects are assigned at random to treatment, and the rest to control. We fit a logit model to data from this randomized controlled experiment, although the model is likely false. The MLE is $\hat{\beta}_n$. ITT and plug-in estimators are defined by (10)–(11).

The size of the population is n . This is increasing to infinity. “Types” of subjects are defined by combinations of possible values for the covariate, the response to control, and the response to treatment. We assume that the fraction of subjects assigned to treatment converges to a positive limit, along with the fraction in each type. The parameters α^T and α^C converge too. This may seem a little odd, but α^T and α^C may depend on the study population, hence on n .

THEOREM 1. *Under the conditions of this section, if a logit model is fitted to data from a randomized controlled experiment: (i) the MLE $\hat{\beta}_n$ converges to a limit β_∞ ; (ii) the plug-in estimator $\hat{\alpha}^T$, the ITT estimator $\hat{\alpha}^T$, and the parameter α^T have a common limit; (iii) $\hat{\alpha}^C$, $\hat{\alpha}^C$, and α^C have a common limit; (iv) $\hat{\Delta}$, $\hat{\Delta}$, and Δ have a common limit. Convergence of estimators holds almost surely, as the sample size grows.*

Estimating Individual-Level Parameters

At the beginning of the paper, it was noted that the individual-level parameters Y_i^T and Y_i^C are estimable. The proof is easy. Recall that $X_i = 1$ if i is assigned to treatment, and $X_i = 0$ otherwise; furthermore, $P(X_i = 1) = \pi_T$ is in $(0, 1)$. Then $Y_i X_i / \pi_T$ is an unbiased estimator for Y_i^T , and $Y_i(1 - X_i) / (1 - \pi_T)$ is an unbiased estimator for Y_i^C , where $Y_i = X_i Y_i^T + (1 - X_i) Y_i^C$ is the observed response.

9. AN INEQUALITY

Let subject i have probability of success p_i if treated, q_i if untreated, with $0 < q_i < 1$ and the q_i not all equal. Suppose

$$\frac{p_i}{1 - p_i} = \lambda \frac{q_i}{1 - q_i}$$

for all i , where $\lambda > 1$. Thus,

$$p_i = \frac{\lambda q_i}{1 + (\lambda - 1)q_i}$$

and $0 < p_i < 1$. Let $\bar{p} = \frac{1}{n} \sum_i p_i$ be the average value of p_i , and likewise for \bar{q} . We define the *pooled multiplier* as

$$\frac{\bar{p}/(1 - \bar{p})}{\bar{q}/(1 - \bar{q})}.$$

The log of this quantity is analogous to the differential log odds in (2).

The main object in this section is showing that

(29) λ is strictly larger than the pooled multiplier.

Russ Lyons suggested this elegant proof. Fix $\lambda > 1$. Let $f(x) = x/(1 - x)$ for $0 < x < 1$. So f is strictly increasing. Let $h(x) = f^{-1}(\lambda f(x))$, so $p_i = h(q_i)$. Inequality (29) says that $f(\bar{p}) < \lambda f(\bar{q})$, that is, $\bar{p} < h(\bar{q})$. Since $p_i = h(q_i)$, proving (29) comes down to proving that h is strictly concave. But

$$\begin{aligned} h(x) &= \frac{\lambda x}{1 + (\lambda - 1)x} \\ &= \frac{\lambda}{\lambda - 1} \left(1 - \frac{1}{1 + (\lambda - 1)x} \right), \end{aligned}$$

and $y \rightarrow 1/y$ is strictly convex for $y > 0$. This completes the proof of (29).

In the other direction,

$$(30) \quad \frac{\bar{p}}{1 - \bar{p}} - \frac{\bar{q}}{1 - \bar{q}} = \frac{\bar{p} - \bar{q}}{(1 - \bar{p})(1 - \bar{q})} > 0$$

because $p_i > q_i$ for all i . So the pooled multiplier exceeds 1. In short, given the assumptions of this section, pooling moves the multiplier downward towards 1. Of course, if $\lambda < 1$, we could simply interchange p and q . The conclusion: pooling moves the multiplier toward 1.

In this paper, we are interested in estimating differential log odds. If the logit model (4) is right, the coefficient β_2 of the treatment indicator is a biased estimator of the differential log odds Δ in (2)—biased away from 0. That is what the inequalities of this section demonstrate, the assumptions being $\beta_3 \neq 0$, Z_i is nonrandom, and Z_i shows variation across i . (Random Z_i are easily accommodated.)

If the logit model is wrong, the inequalities show that $\hat{\beta}_2 > \hat{\Delta}$ if $\hat{\Delta} > 0$, while $\hat{\beta}_2 < \hat{\Delta}$ if $\hat{\Delta} < 0$. The assumptions are the same, with β_3 replaced by $\hat{\beta}_3$, attention being focused on the limiting values defined in the previous section. Since the plug-in estimator $\hat{\Delta}$ is consistent, $\hat{\beta}_2$ must be inconsistent.

The pooling covered by (29)–(30) is a little different from the collapsing discussed in Guo and Geng (1995). (i) Pooling does not involve a joint distribution for $\{X_i, Z_i\}$, or a logit model connecting Y_i to X_i and Z_i . (ii) Guo and Geng consider the distribution of one triplet $\{Y_i, X_i, Z_i\}$ only, that is, $n = 1$.

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