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MS Applied 2017

1. ***a) Determine the mean number of previous pregnancies per woman. (Report the value rounded to 2 decimal places.)***

$$mean = \frac{sum(ppnum)}{\#\ ID's} = \frac{679}{453} \approx 1.50\ pregnancies/woman$$

b) In other studies, the distribution of the number of previous pregnancies is approximated reasonably well by the Poisson distribution. Assuming a Poisson distribution having the mean calculated in part (a), how many women in this dataset would one expect to have had at least 4 previous pregnancies? Test whether the observed number differs significantly from the expected number.

Note: Must assume data is not subject to overdispersion due to a data mean that is very different than the data variance. If it was, would be better to model with a negative binomial instead of a Poisson (which has identical mean and variance).

Using the pmf of the Poisson distribution, we can calculate the proportion of women with at least 4 pregnancies as $1 - \sum_{x=0}^{3} \frac{\exp(-1.5)(1.5)^x}{x!} = 1 - 0.93436 = 0.06564$ or at least 30 (0.06564*453) women.

Use z-test for proportions to determine whether the observed proportion differs significantly from the expected proportion:

$H_0: p_1 - p_2 = 0$

$$Z = \frac{(p_1 - p_2) - 0}{\sqrt{\frac{p_1(1-p_1)}{n_1} + \frac{p_2(1-p_2)}{n_2}}} = \frac{(0.06564 - 0) - 0}{\sqrt{\frac{0.06564(1-0.06564)}{453} + \frac{0(1-0)}{453}}} \approx 5.64$$

Z=-5.6

Assuming a significance level of $\alpha = 0.05$ and two-sided testing, have $Z = 5.64 > 1.96$. Thus, we reject the null hypothesis that the proportions are equivalent. We conclude that the observed number of pregnancies is significantly lower than expected.

Note, you can also do the above problem using a chi-squared test. If you square my answer, you should get your chi-squared value. I am just lazy and think z-scores are easier to calculate (and I know the default critical value, so why not use it).

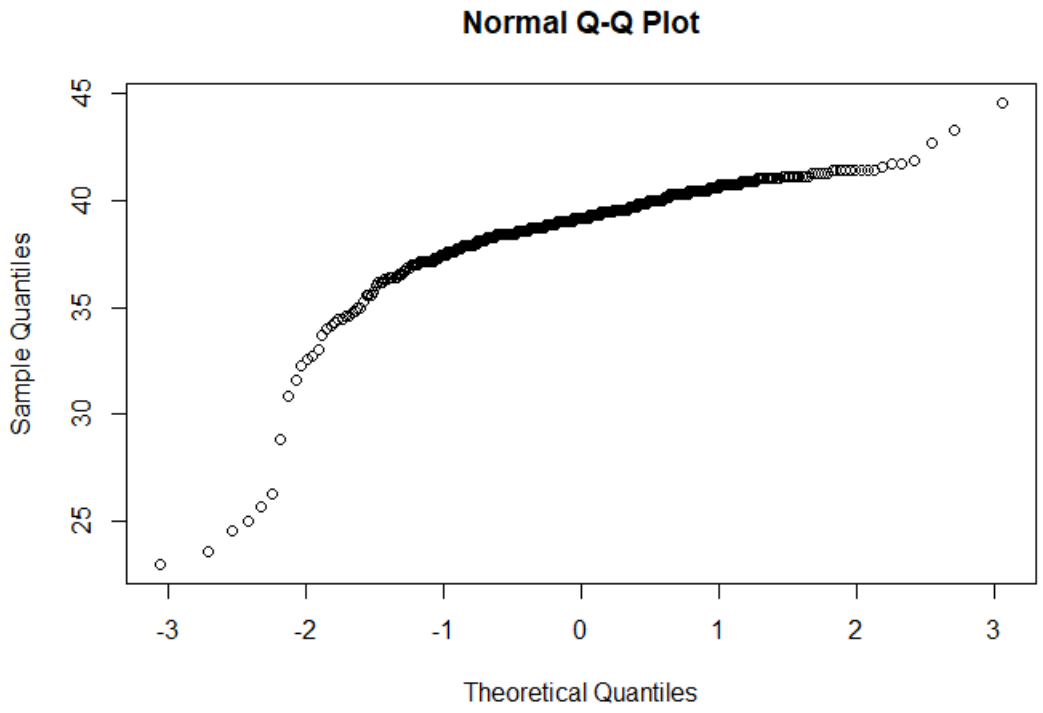
c) Test whether the normal distribution is a good model for the distribution of the ultrasound version of GA.

Will use the Shapiro-Wilk test and q-q plot to determine if the data is approximately normally distributed.

Implementing this test in R using the shapiro.test function, we produce the test statistic W = 0.74326 with p-value < 2.2e-16. Assuming a significance level of $\alpha = 0.05$, we reject the null

hypothesis that the data comes from a normal distribution and conclude that the normal distribution is NOT a good model for the ultrasound version of GA.

In addition to the Shapiro-Wilk test, we can visualize the data by producing a quantile-quantile (q-q) plot, as in the below figure. Note the heavy tails since the outer parts of the curve are steeper than the middle part. This plot is in agreement with our earlier conclusion, that this data would not be modeled well with a normal distribution.



d) Classify both versions of gestational age into 3 intervals, (0,37), [37,40), and [40,∞). Determine how well the two versions agree and provide a 95% confidence interval for the true agreement.

We will estimate the Cohen's kappa statistic to test the null hypothesis that the extent of agreement is the same as random agreement (i.e., kappa=0).

Utilized the Kappa.test() function in the fmsb package in R to produce both the statistic and accompanying 95% CI.

Result:

$\kappa \approx 0.69$ with $p < 2.2e-16$

$95\%\ CI = (0.628, 0.752)$

Using a significance level of $\alpha = 0.05$, since the p-value is well below 0.05, and since we are 95% confident that the true value for the kappa statistic falls somewhere in the interval from 0.628

to 0.752 (not close to including 0), we can conclude that there is moderate to substantial agreement between the two versions of gestational age (after classifying into three intervals).

e) Does the risk of preterm delivery vary monotonically with the number of previous pregnancies?

Use Chi-squared test for trend.

$H_0: \pi_0 = \pi_1 = \pi_2 = \pi_3$ vs. $H_1: \pi_0 \leq \pi_1 \leq \pi_2 \leq \pi_3$ or $H_1: \pi_0 \geq \pi_1 \geq \pi_2 \geq \pi_3$with at least one strict inequality and where 3 is the maximum number of observed pregnancies in the dataset.

Calculation of Test Statistic:

$X^2_{trend} = 2.18$ (see R code)

Critical Region: $C_{0.05} = \{X^2_{trend}: X^2_{trend} > \chi^2_{3,0.95} = 7.82\}$ (via Chi-Square table)

P-value: p=0.54 (see R code)

Conclusion: Assuming a significance level of $\alpha = 0.05$, we fail to reject the null hypothesis. We conclude that the risk of preterm delivery does NOT appear to vary monotonically with the number of previous pregnancies.

f) Based on this study, is treating periodontal disease in pregnant women effective in terms of reducing the risk of prematurity?

Use a chi-squared test to determine if the proportions of women with preterm delivery is the same in women treated for periodontal disease while pregnant versus those treated for periodontal disease post-delivery.

Assumptions for chi-squared test:

- Categories are mutually exclusive and each participant contributes to one, and only one, cell.
- The value of the expecteds should be 5 or more in at least 80% of the cells and no cell should have an expected of less than 1.

$H_0: \pi_1 = \pi_2$ vs $H_1: \pi_1 \neq \pi_2$

where π_1 is the proportion of women with preterm delivery in the prenatal group and π_2 is the proportion of women with preterm delivery in the postnatal group.

$X^2 = 0.426$ (below code)

df = (nrow-1)*(ncol-1) = (2-1)*(2-1) = 1

Critical Region: $C_{0.05} = \{X^2: X^2 > \chi^2_{1,0.95} = 3.84\}$

P-value: p = 0.514 (see uploaded code)

Conclusion: Assuming a significance level of $\alpha = 0.05$, we fail to reject the null hypothesis. We conclude that the intervention does not appear to be successful in reducing the risk of prematurity in pregnant women.

(g) For the prenatal treatment group, did the mean average pocket depth change from baseline to after delivery?

Want to compare mean change within a participant, so use either a paired t-test (parametric) or a Wilcoxon signed rank test (non-parametric) depending on the data distribution. Since the sample size is large (n=368, excluding missingness), we can rely on CLT and Slutsky's and it would be acceptable to use a paired t-test.

$H_0: \mu_{diff} = 0$ vs $H_1: \mu_{diff} \neq 0$

Where μ_{diff} is the difference between the average pocket depth from post-delivery to baseline.

Test statistic: $t = \frac{\bar{x}-\mu}{s/\sqrt{n}} = \frac{-0.00337733-0}{0.4993049/\sqrt{176}} \approx -0.08974$ (verified in R)

Critical Region: $C_{0.05} = \{t: |t| > t_{175,0.05} = 1.97\}$

P-value: p=0.929 (from R)

Conclusion: Assuming a significance level of $\alpha = 0.05$, since the p-value of 0.929 is well above 0.05, we fail to reject the null hypothesis. We conclude that there is no evidence of a significant increase in the mean average pocket depth from baseline to after delivery.

(h) Did the mean change in average pocket depth differ between the two treatment groups?

Want to compare a mean change between groups. For this, we would use either an unpaired t-test (parametric) or a Wilcoxon rank sum test (non-parametric).

Since the sample size is large can rely on CLT and Slutsky's, so it is OK to use two-sample t-test.

$H_0: \mu_{diff1} = \mu_{diff2}$ vs $H_1: \mu_{diff1} \neq \mu_{diff2}$

Where μ_{diff1} is the difference between the average pocket depth from post-delivery to baseline in the prenatal group and μ_{diff2} is the difference between the average pocket depth from post-delivery to baseline in the postpartum group

Test statistic: $t = \frac{(\bar{x}_1-\bar{x}_2)-(0-0)}{\sqrt{\frac{var(\bar{x}_1)}{n_1}+\frac{var(\bar{x}_2)}{n_2}}} \approx -3.63$ (verified in R)

Critical Region: $C_{0.05} = \{t: |t| > t_{346,0.05} = 1.97\}$

P-value: p=0.0003 (from R)

Conclusion: Assuming a significance level of $\alpha = 0.05$, since the p-value of 0.0003 is well below 0.05, we reject the null hypothesis. We conclude that there is a significant difference in the mean change in average pocket depth between the two treatment groups. The prenatal treatment group saw a slight improvement in periodontal disease (decrease in pocket depth of -0.003 mm) from pre- to post- delivery. However, the postnatal treatment group saw a

worsening in periodontal disease (increase in pocket depth of 0.17 mm) from pre- to post-delivery.

(i) Based on the data on average pocket depth, discuss the effectiveness of the periodontal therapy and the consequences for the potential to affect birthweight.

The data suggests that periodontal therapy is not effective in reducing the risk of prematurity in women who are provided dental intervention while pregnant. However, while the intervention did not seem to help the child, it did, however, appear to have helped the mother. Those who received periodontal treatment while pregnant had improved periodontal outcomes after childbirth compared to those who received periodontal treatment postpartum.

2. (a) The researchers would like to first verify whether the mean response in patients receiving chemotherapy differs across clinical subtypes. Please use cell means coding for this section.

i. Write a linear model in matrix notation (using cell means coding) to evaluate this question. Specify the dimension of each component in your model.

No intercept in cell means coding scheme:

$$y_{168\times1} = X_{168\times2}\beta_{2\times1} + \varepsilon_{168\times1}$$

$$\begin{bmatrix} y_1 \\ \vdots \\ n_1 \\ \vdots \\ y_{168} \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ \vdots & \vdots \\ 1 & 0 \\ 0 & 1 \\ \vdots & \vdots \\ 0 & 1 \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \vdots \\ \varepsilon_{168} \end{bmatrix}$$

where X is full rank 2, n_1 is the sample size in the HR+/HER2+ group (level=1), β_1 is the coefficient corresponding to the HR+/HER2+ group, and β_2 is the coefficient corresponding to the HR-/HER2+ group.

ii. Fit this linear model and interpret the coefficients. Then, evaluate whether mean response in patients receiving chemotherapy differs across clinical subtypes.

Model fit as in the above matrix notation using R code (see uploaded code). Since a cell means model does not include an intercept, the coefficients correspond to the two levels of the β vector.

The estimate of 63.3 for the HR+/HER2+ subtype indicates that 63.3% of the tumor remains in chemo patients with this subtype. The estimate of 90.1 for the HR-/HER2+ subtype indicates that 90.1% of the tumor remains in chemo patients with this subtype.

Since the design is unbalanced (121 patients with HR+ and 47 patients with HR- subtype), we will employ a Tukey Honest Significant Differences (HSD) test, which incorporates an adjustment for sample size that produces sensible intervals for mildly unbalanced designs. There is a significant mean difference between the HR- and HR+ subtype is 26.8% (adjusted p-value = 1e-07).

iii. The researchers hypothesize that the variance in chemotherapy response may be larger in the HR+/HER2+ group compared to the HR-/HER2+ group. Evaluate whether the variance in chemotherapy response is homogeneous across clinical subtypes, reporting the test, test statistic, df, p-value for the test, and your interpretation of the result. What additional steps should be taken given your test result, if any?

Use Levene's test to test for homogeneity of variance using the leveneTest() function in R.

$F = 0.8171 \sim F_{1,166}$

$p = 0.37$

Assuming a significance level of $\alpha = 0.05$, since p=0.37 (>0.05), we fail to reject the null hypothesis that there is homogeneity between the groups. Thus, we can safely use hypothesis tests that require the groups have relatively equal variance.

iv. Traditionally, the mean response to chemotherapy among HR+/HER2+ patients has been shown to be twice that of HR-/HER2+ patients. Evaluate whether this relation holds in this study. Write the H0, HA, C, β and θ0 for carrying out this test in the GLH testing framework. Carry out this test and report the test statistic, its df and p-value. Does this result agree with or contradict previous results?

$\mathrm{H}_0: 2\beta_1 = \beta_2$ vs. $\mathrm{H}_0: 2\beta_0 \neq \beta_1$

$$\mathrm{C} = (2, -1), \quad \beta = \begin{pmatrix} \beta_1 \\ \beta_2 \end{pmatrix} \quad \theta_0 = 0$$

Here $\hat{\theta} = C\hat{\beta} = (2, -1)\begin{pmatrix} 63.319 \\ 90.071 \end{pmatrix} = 36.567$

$$F = \frac{\{(\hat{\theta} - \theta_0)'[C(X'X)^{-1}C']^{-1}(\hat{\theta} - \theta_0)/Rank(C)\}}{SSE/dfE}$$

$$= \frac{\left\{(36.567)'\left[(2, -1)\begin{pmatrix} 1/121 & 0 \\ 0 & 1/47 \end{pmatrix}(2, -1)'\right]^{-1}(36.567)/1\right\}}{130712/166}$$

$$\approx 31.25 \sim F_{1,166}$$

P-value computed using `pf(31.25331,1,166,lower.tail=T)` in R gives p=9.13e-08, thus we reject the null hypothesis.

The above by-hand solution was also verified in R using the linearHypothesis function in the car package.

This result agrees with the previous results, which found the mean response to chemotherapy among HR+/HER2+ patients to be only 1.42x (not quite 2x) that of HR-/HER2+ patients.

v. Calculate the estimated covariance between ˆ β1 and ˆ β2. Explain how one may arrive at this result without access to computer software.

Can use the vcov() function in R to get the variance-covariance matrix,

$$\mathrm{Cov}(\hat{\beta}_1, \hat{\beta}_2) = \begin{pmatrix} 6.51 & 0 \\ 0 & 16.75 \end{pmatrix}$$

The correlation between the two coefficients can by computed, by hand, using the below formula:

$$\mathrm{Cov}(\hat{\beta}_1, \hat{\beta}_2) = \hat{\sigma}^2 (X'X)^{-1}$$

where $\hat{\sigma}^2$ is the MSE and $(X'X)^{-1}$ is the SSCP.

(b) Next, the researchers hypothesize that the relative effectiveness of chemotherapy versus hormone therapy may vary across subtypes. That is, the difference in mean response between patients receiving chemotherapy and those receiving hormone therapy may not be the same across subtypes.

i. With respect to clinical subtypes, evaluate this claim by first choosing an appropriate model. Then write out the H0, HA, C, β and ϑ0 for carrying out this test in the GLH testing framework with your chosen model. Carry out this test and interpret the result. Based on the fitted model, suggest which therapy may be better for each clinical subtype and why.

Two-way Factorial Design

	Hormone Therapy	Chemotherapy	
HR+/HER2+	μ_{11}	μ_{12}	$\mu_{1\cdot}$
HR-/HER2+	μ_{21}	μ_{22}	$\mu_{2\cdot}$
	$\mu_{\cdot 1}$	$\mu_{\cdot 2}$	$\mu_{\cdot\cdot}$

METHOD 1: (Reference Cell Coding)

$y_{ijk} = \mu + \alpha_i + \beta_j + \gamma_{ij} + e_{ijk}$

where $i = 2$ corresponds to HR-/HER2 subtype (1 is reference), $j = 2$ corresponds to chemotherapy (1 is reference), and γ_{ij} is the interaction between subtype and treatment.

Clinical Subtype	Treatment	Mean
HR+/HER2+	Hormone Therapy	μ
HR+/HER2+	Chemotherapy	$\mu + \beta_2$
HR-/HER2+	Hormone Therapy	$\mu + \alpha_2$
HR-/HER2+	Chemotherapy	$\mu + \alpha_2 + \beta_2 + \gamma_{22}$

$$\mu_1 = \frac{1}{2}(2\mu + \beta_2) = \mu + \frac{1}{2}\beta_2$$

$$\mu_2 = \frac{1}{2}(2\mu + 2\alpha_2 + \beta_2 + \gamma_{22}) = \mu + \alpha_2 + \frac{1}{2}\beta_2 + \frac{1}{2}\gamma_{22}$$

$$H_0: \mu_1 = \mu_2 \Leftrightarrow \alpha_2 + \frac{1}{2}\gamma_{22} = 0$$

$$H_A: \mu_1 \neq \mu_2 \Leftrightarrow \alpha_2 + \frac{1}{2}\gamma_{22} \neq 0$$

$$C = \begin{bmatrix} 0 & 1 & 0 & \frac{1}{2} \end{bmatrix}, \quad \beta = \begin{bmatrix} \mu \\ \alpha_2 \\ \beta_2 \\ \gamma_{22} \end{bmatrix}, \quad \theta_0 = 0$$

METHOD 2: (Cell Means Coding)

$$\mathrm{Y_{ijk}} = \gamma_{\mathrm{ij}}$$

where γ_{ij} is the interaction between subtype and treatment.

Clinical Subtype	Treatment	Mean
HR+/HER2+	Hormone Therapy	γ_{11}
HR+/HER2+	Chemotherapy	γ_{12}
HR-/HER2+	Hormone Therapy	γ_{21}
HR-/HER2+	Chemotherapy	γ_{22}

$$\mu_1 = \frac{1}{2}(\gamma_{11} + \gamma_{12})$$

$$\mu_2 = \frac{1}{2}(\gamma_{21} + \gamma_{22})$$

$$H_0 = \frac{1}{2}(\gamma_{11} + \gamma_{12}) = \frac{1}{2}(\gamma_{21} + \gamma_{22}) \Leftrightarrow (\gamma_{11} + \gamma_{12}) - (\gamma_{21} + \gamma_{22}) = 0$$

$$H_A = \frac{1}{2}(\gamma_{11} + \gamma_{12}) \neq \frac{1}{2}(\gamma_{21} + \gamma_{22}) \Leftrightarrow (\gamma_{11} + \gamma_{12}) - (\gamma_{21} + \gamma_{22}) \neq 0$$

$$C = [1 \quad 1 \quad -1 \quad -1], \quad \beta = \begin{bmatrix} \gamma_{11} \\ \gamma_{12} \\ \gamma_{21} \\ \gamma_{22} \end{bmatrix}, \quad \theta_0 = 0$$

In R, using a two-way ANOVA for an **unbalanced design** (type = III instead of the default), we find that the interaction between treatment and clinical subtype is significant (F=26.5, p=4.8e-07). *Note: when data is balanced, the factors are orthogonal, and types I, II and III all give the same results.* This implies that the difference in mean response between patients receiving chemotherapy and those receiving hormone therapy may not be the same for those with the HR+/HER2+ subtype versus those with the HR-/HER2+ subtype.

Based on the fitted model, we can perform a Tukey's HSD (honest significant differences) test to determine which type of treatment is beneficial for each subtype. This test assumes there are equal variance between the groups and incorporates an adjustment for sample size in unbalanced designs.

Note that, in the following, a negative difference implies the first type is better at reducing tumor volume and a positive difference implies the second type is better at reducing tumor volume.

If a patient is HR+/HER2+, it appears that s/he would benefit more from chemotherapy than hormone therapy (Chemo:HR+ - Hormone:HR+ = -19.01, p-adj=1.21e-05).

If a patient is HR-/HER2+, it appears that s/he would benefit more from hormone therapy than chemotherapy (Chemo:HR- - Hormone:HR- = 10.38, p-adj=0.06). However, this difference was not statistically significant at a significance level of $\alpha = 0.05$.

ii) Next, the researchers would like to evaluate whether molecular subtype is better at explaining response to treatment than clinical subtype. Fit the same model as the prior sub-part, except this time using molecular subtype instead of clinical subtype. Report the R2 from each model. Can we use R2 to help choose between the two models? Why or why not? If no, propose an alternative measure and use it to help suggest which model may be more appropriate.

R-squared for model in i): $R^2 = 0.17$

R-squared for model in ii): $R^2 = 0.58$

We cannot use R-squared to help us choose between the two models because the models are not nested. However, we can use AIC to compare the two non-nested models. The lower the AIC, the better.

AIC for model in i): $AIC = 2734$

AIC for model in ii): $AIC = 2541$

Thus, it may be more appropriate to choose the second model over the first, since its AIC is lower.

iii) Researchers would like to directly test whether the fit of the previous model using clinical subtype is much better than the fit of the model using molecular subtype. Carry out this test. If you cannot carry out this test, explain why.

Although we can use AIC to tell us which model to choose over the other, AIC tells us nothing about the absolute quality of a model, only the quality relative to other models. Thus, if both models have a poor fit, AIC will not give any warning of that. Thus, we cannot evaluate whether clinical subtype provides a "much better" fit than molecular subtype. Perhaps we could use simulations to do so, but of course I'm not going to do that on an exam…

3.

(a) Test the null hypothesis that, in non-hypertensive women, low birth weight of the first child is not associated with low birth weight of the second child. Apply the same test to the hypertensive group.

The non-hypertensive group:

	Second born not LBW	Second born LBW
First born not LBW	60	10
First born LBW	20	10

The hypertensive group:

	Second born not LBW	Second born LBW
First born not LBW	48	12
First born LBW	22	18

Chi-squared statistic formula for a 2x2 contingency table:

$$\chi^2 = \frac{(ad-bc)^2(a+b+c+d)}{(a+b)(c+d)(a+c)(b+d)}$$

Non-hypertensive: $\chi^2 = \frac{(ad-bc)^2(a+b+c+d)}{(a+b)(c+d)(a+c)(b+d)} = \frac{(60*10-20*10)^2(60+10+20+10)}{(60+10)(20+10)(60+20)(10+10)} \approx 4.76 \sim \chi_1^2$

Hypertensive: $\chi^2 = \frac{(ad-bc)^2(a+b+c+d)}{(a+b)(c+d)(a+c)(b+d)} = \frac{(48*18-22*12)^2(48+12+22+18)}{(48+12)(22+18)(48+22)(12+18)} \approx 7.14 \sim \chi_1^2$

When a comparison is made between one sample and another, a simple rule is that the degrees of freedom equal (number of columns minus one) x (number of rows minus one) not counting the totals for rows or columns. For our data this gives df = (2-1) x (2-1) = 1.

From the chi-squared table, $\chi^2 = 4.76$ on 1 df and $\alpha = 0.05$ has a p-value in the range 0.025<p<0.05.

From the chi-squared table, $\chi^2 = 7.14$ on 1 df and $\alpha = 0.05$ has a p-value in the range 0.001<p<0.01.

Thus, in both the non-hypertensive and hypertensive groups, low birth weight in the first child is associated with low birth weight in the second child.

(b) Suggest a measure of association between low birth weight of the first child and low birth weight of the second child. Compute a point estimate and a 95% confidence interval for this measure, separately for each group of women.

Suggested measure of association: Relative Risk (RR)

Non-Hypertensive: $RR = \frac{a/(a+b)}{c/(c+d)} = \frac{60/(60+10)}{20/(20+10)} \approx 1.29$

Hypertensive: $RR = \frac{a/(a+b)}{c/(c+d)} = \frac{48/(48+12)}{22/(22+18)} \approx 1.45$

Non-Hypertensive: $SE(\ln(RR)) = \sqrt{\frac{1}{a} + \frac{1}{c} - \frac{1}{a+b} - \frac{1}{c+d}} = \sqrt{\frac{1}{60} + \frac{1}{20} - \frac{1}{70} - \frac{1}{30}} \approx 0.138$

Hypertensive: $SE(\ln(RR)) = \sqrt{\frac{1}{a} + \frac{1}{c} - \frac{1}{a+b} - \frac{1}{c+d}} = \sqrt{\frac{1}{48} + \frac{1}{22} - \frac{1}{60} - \frac{1}{40}} \approx 0.157$

Non-Hypertensive: 95% CI = $\exp(\ln(1.29) \pm 1.96 * 0.138) \approx (0.98, 1.69)$

Hypertensive: 95% CI = $\exp(\ln(1.45) \pm 1.96 * 0.157) \approx (1.07, 1.97)$

Thus, in the non-hypertensive group, women whose first pregnancy was low birthweight are 29% higher risk than average of having a second pregnancy that is also low birthweight. However, the confidence interval for this risk includes 1, we cannot claim that this risk is statistically significant.

In the hypertensive group, women whose first pregnancy was low birthweight are 45% higher risk than average of having a second pregnancy that is also low birthweight. Since the confidence interval for this risk does not include 1, we can claim that this risk is statistically significant.

(c) Test the null hypothesis that, in non-hypertensive women, the risk of low birth weight for the first born child is the same as the risk of low birth weight for the second born child. Apply the same test to the hypertensive group.

$H_0: p_1 - p_2 = 0$ vs. $H_A: p_1 - p_2 \neq 0$

Use unpooled test z-test for two proportions.

Non-hypertensive:

$$Z = \frac{(\hat{p}_1 - \hat{p}_2) - 0}{\sqrt{\frac{\hat{p}_1(1-\hat{p}_1)}{n_1} + \frac{\hat{p}_2(1-\hat{p}_2)}{n_2}}} = \frac{(30/100 - 20/100) - 0}{\sqrt{\frac{\frac{30}{100}\left(1-\frac{30}{100}\right)}{100} + \frac{\frac{20}{100}\left(1-\frac{20}{100}\right)}{100}}} \approx 1.64$$

Hypertensive:

$$Z = \frac{(\hat{p}_1 - \hat{p}_2) - 0}{\sqrt{\frac{\hat{p}_1(1-\hat{p}_1)}{n_1} + \frac{\hat{p}_2(1-\hat{p}_2)}{n_2}}} = \frac{(40/100 - 30/100) - 0}{\sqrt{\frac{\frac{40}{100}\left(1-\frac{40}{100}\right)}{100} + \frac{\frac{30}{100}\left(1-\frac{30}{100}\right)}{100}}} \approx 1.49$$

Assuming $\alpha = 0.05$ on 99 df, have $Z_{crit} = 1.96$. Since both Z-statistics fall below the critical value of 1.96, we know they will have p-values > 0.05. So, we fail to reject the null and conclude that the risk of low birth weight for the first born child is no different from the risk of low birth weight for the second born child in both the non-hypertensive and hypertensive groups.

(d) Test the null hypothesis that the joint distribution of the first and second low birth weight outcomes is the same in the two groups of women.

Null: The two populations follow the same distribution.

Alternative: The two populations have different distributions.

Test: Chi-squared test for homogeneity.

Df: (nrow-1)*(ncol-1) = (4-1)*(2-1) = 3

Note: (don't include totals in your row or columns counts in the above formula)

Observed:

	Non-HTN	HTN	Totals
1st normal, 2nd normal	60	48	108
1st normal, 2nd low	10	12	22
1st low, 2nd normal	20	22	42
1st low, 2nd low	10	18	28
Totals	100	100	200

Expected:

	Non-HTN	HTN
1st normal, 2nd normal	(100/200)*108 = 54	(100/200)*108 = 54
1st normal, 2nd low	(100/200)*22 =11	(100/200)*22 = 11
1st low, 2nd normal	(100/200)*42 = 21	(100/200)*42 = 21
1st low, 2nd low	(100/200)*28 = 14	(100/200)*28 = 14

$\chi^2 = \frac{(60-54)^2}{54} + \frac{(48-54)^2}{54} + \frac{(10-11)^2}{11} + \frac{(12-11)^2}{11} + \frac{(20-21)^2}{21} + \frac{(22-21)^2}{21} + \frac{(10-14)^2}{14} + \frac{(18-14)^2}{14} \approx 3.896$
(checked in R as well)

P-value: (for $\alpha = 0.05$ on 3 df from chi-squared table): 0.25 < p < 0.50

(checked in R as well, exact p-value was 0.2729)

Conclusion: Assuming a significance level of $\alpha = 0.05$ (chi-squared test is one-sided), since 0.25<p<0.50 we fail to reject the null hypothesis. We conclude that the non-hypertensive and hypertensive groups are likely to follow the same distribution.

e) The data from only the first child (200 births) were used to fit a logistic regression model (using maximum-likelihood) with low birth weight as response and an indicator of hypertension (x = 0 if non-hypertensive, x = 1 if hypertensive) as a covariate,

logitP(low birth weight) = β1 + β2x.

To the extent possible, present a table of parameter and standard error estimates of β1 and β2. (Remember: only a calculator is allowed).

Construct new contingency table for only first child births:

	Non-HTN	*HTN*	*Total*
First born not LBW	60+10 = 70	48+12 = 60	130
First born LBW	20+10 = 30	22+18 = 40	70
Total	100	100	200

For β_1:

$$logit[P(\text{LBW in Non-HTN})] = \beta_1 + \beta_2(0) = logit\left(\frac{30}{100}\right) = \log\left(\frac{\frac{30}{100}}{1-\frac{30}{100}}\right) \approx -0.847$$

For β_2:

$$logit[P(\text{LBW in HTN})] - logit[P(\text{LBW in Non-HTN})] = (\beta_1 + \beta_2(1)) - (\beta_1 + \beta_2(0)) =$$

$$logit\left(\frac{40}{100}\right) - logit\left(\frac{30}{100}\right) = \log\left(\frac{\frac{0.4}{(1-0.4)}}{\frac{0.30}{1-0.30}}\right) \approx 0.442$$

For SE's, need chi-squared value:

$$X^2 = \frac{(ad-bc)^2(a+b+c+d)}{(a+b)(c+d)(a+c)(b+d)} = \frac{(70*40-60*30)^2(70+60+30+40)}{(70+60)(30+40)(70+30)(60+40)} \approx 2.198 \sim \chi_1^2$$

Then, since, in general, $\sqrt{\chi^2} = Z \approx \frac{\widehat{\beta}}{SE(\widehat{\beta})}$, then

$$SE(\hat{\beta}_1) \approx \frac{\hat{\beta}_1}{\sqrt{X^2}} = \frac{|-0.847|}{\sqrt{2.198}} \approx 0.571$$

$$SE(\hat{\beta}_2) \approx \frac{\hat{\beta}_2}{\sqrt{X^2}} = \frac{0.442}{\sqrt{2.198}} \approx 0.298$$

Thus,

	Estimate	**Standard Error**
$\widehat{\boldsymbol{\beta}}_{\mathbf{1}}$	-0.847	0.571
$\widehat{\boldsymbol{\beta}}_{\mathbf{2}}$	0.442	0.298

(f) Consider the following model:

logitP(low birth weight) = γ1 −γ2x + γ3z − γ4z∗x,

where z is an indicator for the first child (z = 1 for the first child, z = 0 for the second child). Interpret γ3 and γ4. (Notice the negative signs in the model equation.)

For this problem, I am assuming that the gammas have positive value.

If $z = 1$ and $x = 1$, then we increase the odds that $Y = 1$ by a factor of $\exp(\gamma_1 - \gamma_2 + \gamma_3 - \gamma_4)$, or increase the log odds that $Y = 1$ by an increment of $\gamma_1 - \gamma_2 + \gamma_3 - \gamma_4$. In this increment, γ_3 increases the probability of LBW and γ_4 decreases the probability of LBW.

If $z = 1$ and $x = 0$, then we increase the odds that $Y = 1$ by a factor of $\exp(\gamma_1 + \gamma_3)$, or increase the log odds that $Y = 1$ by an increment of $\gamma_1 + \gamma_3$. In this increment, γ_3 increases the probability of LBW.

γ_3 is a coefficient on a main effect.

γ_4 is a coefficient on an interaction.

(g) An investigator suggested using all the data (400 births) in PROC LOGISTIC in SAS to fit the above model to obtain estimates, confidence intervals, p-values, etc. Comment on this suggestion.

It would be problematic to use all of the data because each mother would have two measures (first and second birth). This would violate the model independence assumption because these data would be more similar (correlated) than first/second births for other women. Thus, I would suggest that the investigator control account for this by adding a random effect to the model.