



**JARAMOGI OGINGA ODINGA UNIVERSITY OF SCIENCE AND TECHNOLOGY
SCHOOL OF HEALTH SCIENCES**

UNIVERSITY EXAMINATION FOR DEGREE OF MASTER PUBLIC HEALTH

1ST YEAR 2ND SEMESTER 2022/2023 ACADEMIC YEAR

KISUMU CAMPUS

COURSE CODE: HES 5123

COURSE TITLE: ADVANCED BIostatISTICS

EXAM VENUE:

STREAM: (MPH)

DATE:

EXAM SESSION:

TIME:

3.00 HOURS

Instructions:

1. Answer **Question ONE (compulsory)** and any other **THREE** questions.
2. Candidates **MUST** not to write anything on the question paper.
3. Candidates **MUST** hand in their answer booklets to the invigilator while in the examination room.

SECTION A

Answer question one(Compulsory)

1. Question one (10 marks).

- a) Show that $se(\hat{\pi}) = \frac{1}{\sqrt{-l''(\hat{\pi})}}$ where $se(\hat{\pi})$ is the standard error of the estimated population prevalence and $l''(\hat{\pi})$ is the second derivative of the log-likelihood function of the estimated population prevalence. (3 marks)
- b) Show invariance of Maximum likelihood Estimator *If $\theta = f(\pi)$, then $\hat{\theta} = f(\hat{\pi})$.* (2 marks)

- c) Derive the Wool's formulae for log odds $se[\log(\hat{\Omega})] = \sqrt{\frac{1}{x} + \frac{1}{n-x}}$ for X being the number of individuals with disease, $se[\log(\hat{\Omega})]$ is the standard error of the log-odds and n is the sample size. (3 marks)
- d) Hence similarly for (c) above show that $se[\log(\hat{\pi})] = \sqrt{\frac{1-\hat{\pi}}{n\hat{\pi}}}$. (2 marks)

SECTION B

Answer any three Questions

2. Question two (20 marks).

In a randomized trial patients infected by helicobacter pylori were randomly allocated to treatment by drug combination A or treatment by drug combination B. At the end of the study, the non-cure rates are to be compared between the two groups, using the risk difference or the risk ratio as effect measure.

RESIST resistant against one of the drugs in the combination

0 = no, 1 = yes

CURE cured : 1 = not cured, 0 = cured

TREAT treatment : 0 = drug combination A , 1 = drug combination B

Treatment * Cured * Resistant against one of the drugs in the combination Crosstabulation

Count

| Resistant against one of the drugs in the combination | | | Cured | | Total |
|---|--------------|--------------------|------------|-----------|------------|
| | | | cured | not cured | |
| no | Treatment | drug combination A | 111 | 3 | 114 |
| | | drug combination B | 99 | 6 | 105 |
| | Total | | 210 | 9 | 219 |
| yes | Treatment | drug combination A | 90 | 9 | 99 |
| | | drug combination B | 75 | 12 | 87 |
| | Total | | 165 | 21 | 186 |

Some SAS output

Table of TREAT by CURE

```
TREAT(Treatment)    CURE(Cured)
Frequency
Row Pct            ,cured ,not cure, Total
```

| | d | |
|--------------------|----|-----|
| drug combination A | 12 | 213 |
| drug combination B | 18 | 192 |
| Total | 30 | 405 |

Statistics for Table of TREAT by CURE

Column 2 Risk Estimates

| | Risk | ASE | (Asymptotic) 95% Confidence Limits | (Exact) 95% Confidence Limits |
|------------|---------|--------|------------------------------------|-------------------------------|
| Row 1 | 0.0563 | 0.0158 | 0.0254 0.0873 | 0.0294 0.0963 |
| Row 2 | 0.0938 | 0.0210 | 0.0525 0.1350 | 0.0565 0.1441 |
| Total | 0.0741 | 0.0130 | 0.0486 0.0996 | 0.0505 0.1041 |
| Difference | -0.0374 | 0.0263 | -0.0890 0.0142 | |

Difference is (Row 1 - Row 2)

Statistics for Table of TREAT by CURE

Estimates of the Relative Risk (Row1/Row2)

| Type of Study | Value | 95% Confidence Limits | |
|---------------------------|--------|-----------------------|--------|
| Case-Control (Odds Ratio) | 1.7328 | 0.8119 | 3.6981 |
| Cohort (Col1 Risk) | 1.0413 | 0.9845 | 1.1014 |
| Cohort (Col2 Risk) | 0.6009 | 0.2973 | 1.2149 |

Sample Size = 405

Model Information

Data Set WORK.HELIPYL
 Distribution Binomial
 Link Function Identity
 Dependent Variable CURE Cured

Number of Observations Read 405
 Number of Observations Used 405
 Number of Events 30
 Number of Trials 405

Response Profile

| Ordered Value | CURE | Total Frequency |
|---------------|-----------|-----------------|
| 1 | not cured | 30 |
| 2 | cured | 375 |

PROC GENMOD is modeling the probability that CURE='not cured'.

Criteria For Assessing Goodness Of Fit

| Criterion | DF | Value | Value/DF |
|--------------------------|----|-----------|----------|
| Log Likelihood | | -105.9089 | |
| Full Log Likelihood | | -105.9089 | |
| AIC (smaller is better) | | 215.8177 | |
| AICC (smaller is better) | | 215.8476 | |
| BIC (smaller is better) | | 223.8255 | |

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

| Parameter | DF | Estimate | Standard Error | Wald 95% Confidence Limits | Likelihood Ratio 95% Confidence Limits | Wald Chi-Square | Pr > ChiSq |
|-----------|----|----------|----------------|----------------------------|--|-----------------|------------|
| Intercept | 1 | 0.0563 | 0.0158 | 0.0254 0.0873 | 0.0306 0.0927 | 12.72 | 0.0004 |
| TREAT | 1 | 0.0374 | 0.0263 | -0.0142 0.0890 | -0.0137 0.0914 | 2.02 | 0.1550 |
| Scale | 0 | 1.0000 | 0.0000 | 1.0000 1.0000 | 1.0000 1.0000 | | |

NOTE: The scale parameter was held fixed.

Relative risk model

The GENMOD Procedure

Model Information

Data Set WORK.HELIPYL
Distribution Binomial
Link Function Log
Dependent Variable CURE Cured

Number of Observations Read 405
Number of Observations Used 405
Number of Events 30
Number of Trials 405

Response Profile

| Ordered Value | CURE | Total Frequency |
|---------------|-----------|-----------------|
| 1 | not cured | 30 |
| 2 | cured | 375 |

PROC GENMOD is modeling the probability that CURE='not cured'.

Parameter Information

| Parameter | Effect |
|-----------|-----------|
| Prm1 | Intercept |
| Prm2 | TREAT |

Criteria For Assessing Goodness Of Fit

| Criterion | DF | Value | Value/DF |
|--------------------------|----|-----------|----------|
| Log Likelihood | | -105.9089 | |
| Full Log Likelihood | | -105.9089 | |
| AIC (smaller is better) | | 215.8177 | |
| AICC (smaller is better) | | 215.8476 | |
| BIC (smaller is better) | | 223.8255 | |

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

| Parameter | DF | Estimate | Standard Error | Wald 95% Confidence Limits | Likelihood Ratio 95% Confidence Limits | Wald Chi-Square | Pr > ChiSq |
|-----------|----|----------|----------------|----------------------------|--|-----------------|------------|
| Intercept | 1 | -2.8764 | 0.2804 | -3.4260 -2.3268 | -3.4876 -2.3786 | 105.21 | <.0001 |
| TREAT | 1 | 0.5093 | 0.3591 | -0.1947 1.2132 | -0.1844 1.2416 | 2.01 | 0.1562 |
| Scale | 0 | 1.0000 | 0.0000 | 1.0000 1.0000 | 1.0000 1.0000 | | |

NOTE: The scale parameter was held fixed.

Contrast Estimate Results

| Label | Mean Estimate | Mean Confidence Limits | L'Beta Estimate | Standard Error | Alpha | L'Beta Confidence Limits |
|-----------------|---------------|------------------------|-----------------|----------------|-------|--------------------------|
| TreatmentB | 1.6641 | 0.8231 3.3641 | 0.5093 | 0.3591 | 0.05 | -0.1947 1.2132 |
| Exp(TreatmentB) | | | 1.6641 | 0.5976 | 0.05 | 0.8231 3.3641 |

Contrast Estimate Results

| Label | Chi-Square | Pr > ChiSq |
|-----------------|------------|------------|
| TreatmentB | 2.01 | 0.1562 |
| Exp(TreatmentB) | | |

Relative risk model

The FREQ Procedure

Table 1 of TREAT by CURE
Controlling for RESIST=no

| TREAT(Treatment) | CURE(Cured) | Frequency | Row Pct | , cured | , not cure, | Total |
|------------------|-------------|-----------|---------|---------|-------------|-------|
| drug combination | A | 111 | 3 | 114 | | |
| drug combination | B | 99 | 6 | 105 | | |
| Total | | 210 | 9 | 219 | | |

Statistics for Table 1 of TREAT by CURE
Controlling for RESIST=no

Column 1 Risk Estimates

| | Risk | ASE | (Asymptotic) 95% Confidence Limits | (Exact) 95% Confidence Limits |
|------------|--------|--------|------------------------------------|-------------------------------|
| Row 1 | 0.9737 | 0.0150 | 0.9443 1.0000 | 0.9250 0.9945 |
| Row 2 | 0.9429 | 0.0227 | 0.8985 0.9873 | 0.8798 0.9787 |
| Total | 0.9589 | 0.0134 | 0.9326 0.9852 | 0.9234 0.9810 |
| Difference | 0.0308 | 0.0272 | -0.0224 0.0841 | |

Difference is (Row 1 - Row 2)

Column 2 Risk Estimates

| | Risk | ASE | (Asymptotic) 95% Confidence Limits | (Exact) 95% Confidence Limits |
|------------|---------|--------|------------------------------------|-------------------------------|
| Row 1 | 0.0263 | 0.0150 | 0.0000 0.0557 | 0.0055 0.0750 |
| Row 2 | 0.0571 | 0.0227 | 0.0127 0.1015 | 0.0213 0.1202 |
| Total | 0.0411 | 0.0134 | 0.0148 0.0674 | 0.0190 0.0766 |
| Difference | -0.0308 | 0.0272 | -0.0841 0.0224 | |

Difference is (Row 1 - Row 2)

Relative risk model

The FREQ Procedure

Statistics for Table 1 of TREAT by CURE
Controlling for RESIST=no

Estimates of the Relative Risk (Row1/Row2)

| Type of Study | Value | 95% Confidence Limits |
|---------------------------|--------|-----------------------|
| Case-Control (Odds Ratio) | 2.2424 | 0.5463 9.2045 |
| Cohort (Coll Risk) | 1.0327 | 0.9765 1.0921 |

Cohort (Col2 Risk) 0.4605 0.1182 1.7949

Sample Size = 219

Table 2 of TREAT by CURE
Controlling for RESIST=yes

| TREAT(Treatment) | CURE(Cured) | | Total |
|--------------------|-------------|-------------|-------|
| Frequency | , cured | , not cure, | |
| Row Pct | ,d | ,d | |
| drug combination A | 90 | 9 | 99 |
| | 90.91 | 9.09 | |
| drug combination B | 75 | 12 | 87 |
| | 86.21 | 13.79 | |
| Total | 165 | 21 | 186 |

Statistics for Table 2 of TREAT by CURE
Controlling for RESIST=yes

Column 1 Risk Estimates

| | Risk | ASE | (Asymptotic) 95% Confidence Limits | (Exact) 95% Confidence Limits |
|------------|--------|--------|---------------------------------------|----------------------------------|
| Row 1 | 0.9091 | 0.0289 | 0.8525 0.9657 | 0.8344 0.9576 |
| Row 2 | 0.8621 | 0.0370 | 0.7896 0.9345 | 0.7715 0.9266 |
| Total | 0.8871 | 0.0232 | 0.8416 0.9326 | 0.8326 0.9287 |
| Difference | 0.0470 | 0.0469 | -0.0449 0.1390 | |

Difference is (Row 1 - Row 2)

Relative risk model

The FREQ Procedure

Statistics for Table 2 of TREAT by CURE
Controlling for RESIST=yes

Column 2 Risk Estimates

| | Risk | ASE | (Asymptotic) 95% Confidence Limits | (Exact) 95% Confidence Limits |
|------------|---------|--------|---------------------------------------|----------------------------------|
| Row 1 | 0.0909 | 0.0289 | 0.0343 0.1475 | 0.0424 0.1656 |
| Row 2 | 0.1379 | 0.0370 | 0.0655 0.2104 | 0.0734 0.2285 |
| Total | 0.1129 | 0.0232 | 0.0674 0.1584 | 0.0713 0.1674 |
| Difference | -0.0470 | 0.0469 | -0.1390 0.0449 | |

Difference is (Row 1 - Row 2)

Estimates of the Relative Risk (Row1/Row2)

| Type of Study | Value | 95% Confidence Limits |
|---------------------------|--------|-----------------------|
| Case-Control (Odds Ratio) | 1.6000 | 0.6396 4.0028 |
| Cohort (Col1 Risk) | 1.0545 | 0.9498 1.1708 |
| Cohort (Col2 Risk) | 0.6591 | 0.2918 1.4888 |

Sample Size = 186

Answer the following questions

- Compute the risk difference and a relative risk. (2 marks)
- Compare the risk of not getting cured with either treatment A or B. Find the risk difference/risk ratio and its confidence interval for the non-cure rate. (hint transformation cure=1). (2 marks)

- c. Compute the Wald's 95%CI. (2 marks)
- d. What is the interpretation of the estimated regression coefficients? (2 marks)
- e. Some of the patients are resistant to one of the drugs in the drug combination, others are not resistant. Adjust the estimates of the risk difference for resistance. (2 marks)
- f. Compute the risk differences in both strata. (4 marks)
- g. Calculate the weighted mean of the two risk difference using the weight factor for each stratum: One over the squared standard error. (4 marks)
- h. Is there evidence of heterogeneity for both RD and RR? (Hint: use interaction term that tests that RD or RR in two strata is equal) (2 marks)

3. Question three (20 marks).

- 1. Presence of a certain element of the set of teeth in babies, depending on age

Y=1/0 if element present/absent

X=age at examination (weeks)

Using binary logistic regression in SPSS gives the following:

Y

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---------|-----------|---------|---------------|--------------------|
| Valid 0 | 38 | 76.0 | 76.0 | 76.0 |
| 1 | 12 | 24.0 | 24.0 | 100.0 |
| Total | 50 | 100.0 | 100.0 | |

Block 0

Variables in the Equation

| | B | S.E. | Wald | Df | Sig. | Exp(B) |
|-----------------|--------|------|--------|----|------|--------|
| Step 0 Constant | -1.153 | .331 | 12.117 | 1 | .000 | .316 |

Iteration History(a,b,c,d)

| Iteration | | -2 Log likelihood | Coefficients | |
|-----------|---|-------------------|--------------|------|
| | | | Constant | X |
| Step 1 | 1 | 36.215 | -3.827 | .095 |
| | 2 | 29.677 | -6.483 | .162 |
| | 3 | 27.743 | -8.796 | .220 |
| | 4 | 27.474 | -10.043 | .251 |
| | 5 | 27.467 | -10.287 | .257 |

| | | | |
|---|--------|---------|------|
| 6 | 27.467 | -10.295 | .257 |
| 7 | 27.467 | -10.295 | .257 |

- a Method: Forward Stepwise (Wald)
- b Constant is included in the model.
- c Initial -2 Log Likelihood: 55.108
- d Estimation terminated at iteration number 7 because parameter estimates changed by less than .001.

Variables in the Equation

| | B | S.E. | Wald | df | Sig. | Exp(B) | 95.0% C.I. for EXP(B) | |
|-------------|---------|-------|--------|----|------|--------|-----------------------|-------|
| | | | | | | | Lower | Upper |
| Step 1(a) X | .257 | .078 | 10.727 | 1 | .001 | 1.293 | 1.109 | 1.508 |
| Constant | -10.295 | 3.066 | 11.275 | 1 | .001 | .000 | | |

- a Variable(s) entered on step 1: X.

Correlation Matrix

| | | Constant | X |
|--------|----------|----------|-------|
| Step 1 | Constant | 1.000 | -.987 |
| | X | -.987 | 1.000 |

- a. Estimate of the covariance matrix, hence what are the standard errors (s_0) and (s_1)? (4 marks)
- b. What is the correlation between $\hat{\beta}_0$ and $\hat{\beta}_1$. (2 marks)
- c. Give the 95%CI for β_1 using the Wald's method. (2 marks)
- d. What is the probability that a 40 week old will have the element?. (8 marks)
- e. Test for $H_0: \beta_1 = 0$ with three methods (follow SPSS output). (4 marks)

4. Question four (20 marks).

- 2. In a random sample from the population of a rural area in a certain developing country the following variables, among others, were observed on 328 persons.

SYS systolic blood pressure (mmHg)

PULSE pulse rate (beats/min)

SES social economic status (1=lower class, 2=middle class, 3=upper class)

This problem concentrates on the differences in mean systolic blood pressure between the three social economic classes corrected for pulse frequency. Three multiple regression models were fitted using SPSS. Part of the output is given below.

Model 1:

Variables Entered/Removed(b)

| Model | Variables Entered | Variables Removed | Method |
|-------|---|-------------------|--------|
| 1 | middle social economic class, low social economic status(a) | . | Enter |

a All requested variables entered.

b Dependent Variable: systolic blood pressure (mmHg)

ANOVA(b)

| Model | | Sum of Squares | df | Mean Square | F | Sig. |
|-------|------------|----------------|-----|-------------|-------|---------|
| 1 | Regression | 4019.437 | 2 | 2009.719 | 6.898 | .001(a) |
| | Residual | 94683.840 | 325 | 291.335 | | |
| | Total | 98703.277 | 327 | | | |

a Predictors: (Constant), middle social economic class, low social economic status

b Dependent Variable: systolic blood pressure (mmHg)

Coefficients(a)

| Model | | Unstandardized Coefficients | | Standardized Coefficients | t | Sig. |
|-------|------------------------------|-----------------------------|------------|---------------------------|---------|------|
| | | B | Std. Error | Beta | | |
| 1 | (Constant) | 126.381 | 1.002 | | 126.175 | .000 |
| | low social economic status | -2.196 | 1.307 | -.095 | -1.681 | .094 |
| | middle social economic class | -3.645 | 1.330 | -.155 | -2.741 | .006 |

a Dependent Variable: systolic blood pressure (mmHg)

Model 2:

Model Summary

| Model | R | R Square | Adjusted R Square | Std. Error of the Estimate |
|-------|---------|----------|-------------------|----------------------------|
| 1 | .169(a) | .029 | .026 | 17.15045 |
| 2 | .258(b) | .067 | .058 | 16.86281 |
| 3 | .259(c) | .067 | .055 | 16.88669 |

a Predictors: (Constant), pulse frequency (beats/min)

b Predictors: (Constant), pulse frequency (beats/min), low social economic status, middle social economic class

c Predictors: (Constant), pulse frequency (beats/min), low social economic status, middle social economic class, squared pulse rate

ANOVA(d)

| Model | | Sum of Squares | df | Mean Square | F | Sig. |
|-------|------------|----------------|-----|-------------|-------|---------|
| 1 | Regression | 2814.288 | 1 | 2814.288 | 9.568 | .002(a) |
| | Residual | 95888.989 | 326 | 294.138 | | |
| | Total | 98703.277 | 327 | | | |
| 2 | Regression | 6572.496 | 3 | 2190.832 | 7.705 | .000(b) |
| | Residual | 92130.781 | 324 | 284.354 | | |
| | Total | 98703.277 | 327 | | | |
| 3 | Regression | 6596.497 | 4 | 1649.124 | 5.783 | .000(c) |
| | Residual | 92106.780 | 323 | 285.160 | | |
| | Total | 98703.277 | 327 | | | |

a Predictors: (Constant), pulse frequency (beats/min)

b Predictors: (Constant), pulse frequency (beats/min), low social economic status, middle social economic class

c Predictors: (Constant), pulse frequency (beats/min), low social economic status, middle social economic class, squared pulse rate

d Dependent Variable: systolic blood pressure (mmHg)

Coefficients(a)

| Model | | Unstandardized Coefficients | | Standardized Coefficients | t | Sig. |
|-------|------------------------------|-----------------------------|------------|---------------------------|--------|------|
| | | B | Std. Error | Beta | | |
| 1 | (Constant) | 104.616 | 6.711 | | 15.588 | .000 |
| | pulse frequency (beats/min) | .250 | .081 | .169 | 3.093 | .002 |
| 2 | (Constant) | 106.752 | 6.625 | | 16.113 | .000 |
| | pulse frequency (beats/min) | .239 | .080 | .161 | 2.996 | .003 |
| | low social economic status | -2.196 | 1.291 | -.095 | -1.701 | .090 |
| 3 | middle social economic class | -3.472 | 1.315 | -.147 | -2.641 | .009 |
| | (Constant) | 97.588 | 32.277 | | 3.024 | .003 |
| | pulse frequency (beats/min) | .464 | .781 | .313 | .594 | .553 |
| | low social economic status | -2.223 | 1.296 | -.096 | -1.715 | .087 |
| | middle social economic class | -3.432 | 1.324 | -.146 | -2.592 | .010 |
| | squared pulse rate | -.001 | .005 | -.153 | -.290 | .772 |

a Dependent Variable: systolic blood pressure (mmHg)

Model 3:

Model Summary

| Model | R | R Square | Adjusted R Square | Std. Error of the Estimate |
|-------|---------|----------|-------------------|----------------------------|
| 1 | .258(a) | .067 | .058 | 16.86281 |
| 2 | .284(b) | .081 | .066 | 16.78795 |

a Predictors: (Constant), middle social economic class, pulse frequency (beats/min), low social economic status

b Predictors: (Constant), middle social economic class, pulse frequency (beats/min), low social economic status, mid_pulse, low_pulse

ANOVA(c)

| Model | | Sum of Squares | df | Mean Square | F | Sig. |
|-------|------------|----------------|-----|-------------|-------|---------|
| 1 | Regression | 6572.496 | 3 | 2190.832 | 7.705 | .000(a) |
| | Residual | 92130.781 | 324 | 284.354 | | |
| | Total | 98703.277 | 327 | | | |
| 2 | Regression | 7952.374 | 5 | 1590.475 | 5.643 | .000(b) |
| | Residual | 90750.903 | 322 | 281.835 | | |
| | Total | 98703.277 | 327 | | | |

a Predictors: (Constant), middle social economic class, pulse frequency (beats/min), low social economic status

b Predictors: (Constant), middle social economic class, pulse frequency (beats/min), low social economic status, mid_pulse, low_pulse

c Dependent Variable: systolic blood pressure (mmHg)

Coefficients(a)

| Model | | Unstandardized Coefficients | | Standardized Coefficients | t | Sig. |
|-------|------------------------------|-----------------------------|------------|---------------------------|--------|------|
| | | B | Std. Error | Beta | | |
| 1 | (Constant) | 106.752 | 6.625 | | 16.113 | .000 |
| | pulse frequency (beats/min) | .239 | .080 | .161 | 2.996 | .003 |
| | low social economic status | -2.196 | 1.291 | -.095 | -1.701 | .090 |
| | middle social economic class | -3.472 | 1.315 | -.147 | -2.641 | .009 |
| 2 | (Constant) | 101.067 | 7.155 | | 14.125 | .000 |
| | pulse frequency (beats/min) | .306 | .086 | .207 | 3.568 | .000 |
| | low social economic status | 12.841 | 9.568 | .554 | 1.342 | .181 |
| | middle social economic class | 6.729 | 9.051 | .285 | .743 | .458 |
| | low_pulse | -.181 | .115 | -.653 | -1.578 | .116 |
| | mid_pulse | -.123 | .109 | -.435 | -1.130 | .259 |

a Dependent Variable: systolic blood pressure (mmHg)

In order to look at the crude differences in mean systolic blood pressure between the three groups, model 1 is fitted. Study the output of model 1, notice in particular how the independent variables are coded (**LOW:1 0 -1 and MID: 0 1 -1**), and answer questions (a) to (d).

- a. What is the interpretation of the estimated regression coefficients of the independent variables “low social economic status” and “middle social economic status”? (1 mark)
 - i. Give also the interpretation of the estimated intercept. (1 mark)
 - ii. Compute the estimates for the mean systolic blood pressure of the three SES classes. (1 mark)
- b. Are there significant differences in mean systolic blood pressures between the SES groups?
 - i. Formulate the null hypothesis and give the p-value. (1 mark)
- c. Give the estimate of the within groups standard deviation of systolic blood pressure. (1 mark)
 - i. How can this be used to compute an (approximate) 95% confidence interval for the group means? (1 mark)
 - ii. Give this confidence interval for the low SES group. (the number of individuals in the lower SES group was 138) (1 mark)
- d. Give the estimate of the percentage variability in systolic blood pressure that is explained by differences between SES classes. (1 mark)

In order to look at the differences in mean systolic blood pressure between the SES groups corrected for pulse rate, model 2 was fitted. Study the output of model 2 and answer the questions (e) and (h).

- e. Are there significant differences in mean systolic blood pressures between the SES groups corrected for pulse rate? (1 mark)
 - i. Formulate the null hypothesis and give the p-value. (2 marks)
- f. Give the estimate of the pulse rate corrected difference in mean systolic blood pressure between the low and middle SES group. (1 mark)
 - i. Do the same for the low and high group and for the middle and high group. (1 mark)
- g. Compute the estimate, based on model 2, of the mean systolic blood pressure for middle class people with pulse rate equal to 70 (1 mark)
- h. One of the assumptions underlying model 2 is that the relation between systolic blood pressure and pulse rate is linear. Is this assumption reasonable in this case? (1 mark)
 - i. Motivate your answer. (1 mark)

One of the assumptions of model 2 is that there is no interaction between SES classes and pulse rate. In order to investigate whether this assumption is justified, model 3 was fitted. Study the output of model 3 and answer the following questions.

- i. Is there statistical evidence that there is interaction between SES class and pulse rate? (1 mark)
 - i. Motivate your answer. (1 mark)
- j. Give the equation of the estimated regression line (based on model 3) of systolic blood pressure against pulse rate for the low SES group. (1 mark)

What is the estimated difference (based on model 3) in mean systolic blood pressure (1 mark)

5. Question five (20 marks).

The table below gives results of 6 clinical trials comparing the risk of OHSS (ovarian hyperstimulation syndrome) between recombinant FSH and urinary FSH used during an IVF (in vitro fertilization) treatment.

| Trial | No. of patients Rec FSH | No. of patients Ur FSH | OHSS Rec FSH | OHSS Ur FSH |
|-------|-------------------------|------------------------|--------------|-------------|
| 1 | 585 | 396 | 19 | 8 |
| 2 | 57 | 33 | 3 | 0 |
| 3 | 54 | 35 | 2 | 1 |
| 4 | 119 | 114 | 6 | 2 |
| 5 | 60 | 63 | 2 | 1 |
| 6 | 105 | 67 | 8 | 3 |

A meta-analysis was carried out using Mantel-Haenszel's procedure, stratified on trial. Some SPSS output is given at the following pages. Read this output and answer the following questions.

Risk Estimate

| Trial | Odds Ratio for FSH (Recombinant / Urinary) | Value | 95% Confidence Interval | |
|-------|--|-------|-------------------------|-------|
| | | | Lower | Upper |
| 1 | | .614 | .266 | 1.417 |

| | | | | |
|---|---|-------|------|--------|
| | For cohort OHSS = no | .987 | .967 | 1.008 |
| | For cohort OHSS = yes | 1.608 | .711 | 3.636 |
| | N of Valid Cases | 981 | | |
| 2 | For cohort OHSS = no | .947 | .891 | 1.007 |
| | N of Valid Cases | 90 | | |
| 3 | Odds Ratio for FSH (Recombinant / Urinary) | .765 | .067 | 8.765 |
| | For cohort OHSS = no | .991 | .918 | 1.071 |
| | For cohort OHSS = yes | 1.296 | .122 | 13.763 |
| | N of Valid Cases | 89 | | |
| 4 | Odds Ratio for FSH (Recombinant / Urinary) | .336 | .066 | 1.702 |
| | For cohort OHSS = no | .967 | .921 | 1.014 |
| | For cohort OHSS = yes | 2.874 | .592 | 13.947 |
| | N of Valid Cases | 233 | | |
| 5 | Odds Ratio for FSH (Recombinant / Urinary) | .468 | .041 | 5.297 |
| | For cohort OHSS = no | .982 | .928 | 1.039 |
| | For cohort OHSS = yes | 2.100 | .195 | 22.561 |
| | N of Valid Cases | 123 | | |
| 6 | Odds Ratio for FSH (Recombinant / Urinary) | .568 | .145 | 2.223 |
| | For cohort OHSS = no | .967 | .897 | 1.043 |
| | For cohort OHSS = yes | 1.702 | .468 | 6.188 |
| | N of Valid Cases | 172 | | |

Tests of Homogeneity of the Odds Ratio

| | Chi-Squared | df | Asymp. Sig. (2-sided) |
|-------------|-------------|----|--------------------------|
| Breslow-Day | 1.507 | 5 | .912 |
| Tarone's | 1.507 | 5 | .912 |

Mantel-Haenszel Common Odds Ratio Estimate

| | | | |
|-----------------------------------|--------------------------|-------------|-------|
| Estimate | | | .513 |
| ln(Estimate) | | | -.668 |
| Std. Error of ln(Estimate) | | | .308 |
| Asymp. Sig. (2-sided) | | | ??? |
| Asymp. 95% Confidence Interval | Common Odds Ratio | Lower Bound | ??? |
| | | Upper Bound | ??? |
| | ln(Common Odds Ratio) | Lower Bound | ??? |
| | | Upper Bound | ??? |

k. Make a 2X2 table for the first trial.

- i. Compute the OHSS odds ratio of recombinant FSH treatment relative to urinary FSH treatment. (1 mark)
- ii. Compute also the corresponding relative risk (1 mark)
- iii. How are these estimates related to the estimates given for trial 1 in the first table of the SPSS output (1 mark)
- iv. What is the difference between the two relative risk estimates? (1 mark)
- l. Give the OHSS odds ratios of recombinant FSH relative to urinary FSH per trial. Is the assumption that the true odds ratios are equal across trials warranted? (7 marks)
 - i. Motivate your answer. (1 mark)
- m. Give the Mantel-Haenzel estimate of the common OHSS odds ratios of recombinant FSH relative to urinary FSH. (2 marks)
 - i. Is it justified to interpret it as a relative risk? (1 mark)
- n. Fill in the question marks in the third table. (5 marks)