Chapter 30

Latin Square and Related Designs

We look at latin square and related designs.

30.1 Basic Elements

Exercise 30.1 (Basic Elements)

1. *Different arrangements of same data.*
   Nine patients are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: age (1: below 25, 2: 25 to 35, 3: above 35) and health (1: poor, 2: fair, 3: good). The following two arrangements of drug responses for age/health/drugs,

health, i:	1			2			3		
age, j:	1	2	3	1	2	3	1	2	3
drugs, $k = 1$ (A):	69				92				44
$k = 2$ (B):		80				47	65		
$k = 3$ (C):			40	91				63	

health ↓ age→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	69 (A)	80 (B)	40 (C)
$i = 2$	91 (C)	92 (A)	47 (B)
$i = 3$	65 (B)	63 (C)	44 (A)

   are (choose one) **the same** / **different** data sets. This is a latin square design and is an example of an *in*complete block design. Health and age are two *blocks* for the treatment, drug.

2. *How is a latin square created?*
   True / **False** Drug treatment A not only appears in all three columns (age block) and in all three rows (health block) but also only appears *once* in every row and column. This is also true of the other two treatments (B, C).

3. *Other latin squares.*
Which are latin squares? Choose none, one or more.

(a) latin square candidate 1

health ↓ age→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	69 (A)	80 (B)	40 (C)
$i = 2$	91 (B)	92 (C)	47 (A)
$i = 3$	65 (C)	63 (A)	44 (B)

(b) latin square candidate 2

health ↓ age→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	69 (A)	80 (C)	40 (B)
$i = 2$	91 (B)	92 (A)	47 (C)
$i = 3$	65 (C)	63 (B)	44 (A)

(c) latin square candidate 3

health ↓ age→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	69 (B)	80 (A)	40 (C)
$i = 2$	91 (C)	92 (B)	47 (B)
$i = 3$	65 (A)	63 (C)	44 (A)

In fact, there are twelve (12) latin squares when $r = 3$. There are 161,280 latin squares when $r = 5$.

4. *Latin squares counteract/reduce order effect*
Nine patients are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: time (1: morning 25, 2: afternoon, 3: evening) and day (1, 2, 3).

day ↓ time→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	69 (A)	80 (B)	40 (C)
$i = 2$	91 (C)	92 (A)	47 (B)
$i = 3$	65 (B)	63 (C)	44 (A)

Since the three drugs are given in a different order during each of the three days, this should (choose one) **decrease** / **increase** any confounding effect due to the time at which any of the drugs are given during the day.

5. *Latin square, with replications.*
Eighteen (18) patients are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: age (1: below 25, 2: 25 to 35, 3: above 35) and health (1: poor, 2: fair, 3: good). Two possible equivalent arrangements of this data are given below.

health ↓	replication, ↓ age→	$j=1$	$j=2$	$j=3$
$i=1$	$l=1$	69 (A)	80 (B)	40 (C)
	$l=2$	68 (A)	89 (B)	62 (C)
$i=2$	$l=1$	91 (C)	92 (A)	47 (B)
	$l=2$	80 (C)	95 (A)	68 (B)
$i=3$	$l=1$	65 (B)	63 (C)	44 (A)
	$l=2$	40 (B)	43 (C)	49 (A)

replication, ↓	health ↓ age→	$j=1$	$j=2$	$j=3$
	$i=1$	69 (A)	80 (B)	40 (C)
$l=1$	$i=2$	91 (C)	92 (A)	47 (B)
	$i=3$	65 (B)	63 (C)	44 (A)
	$i=1$	68 (A)	89 (B)	62 (C)
$l=2$	$i=2$	80 (C)	95 (A)	68 (B)
	$i=3$	40 (B)	43 (C)	49 (A)

There are (choose one) **one** / **two** / **three** replications of this latin square design. Increased replication decreases error variance.

6. *Additional latin squares.*
Eighteen (18) patients are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: age (1: below 25, 2: 25 to 35, 3: above 35) and health (1: poor, 2: fair, 3: good). Two possible equivalent arrangements of this data are given below.

health ↓	latin square, ↓ age→	$j=1$	$j=2$	$j=3$
$i=1$	$l=1$	69 (A)	80 (B)	40 (C)
	$l=2$	68 (A)	89 (C)	62 (B)
$i=2$	$l=1$	91 (C)	92 (A)	47 (B)
	$l=2$	80 (B)	95 (A)	68 (C)
$i=3$	$l=1$	65 (B)	63 (C)	44 (A)
	$l=2$	40 (C)	43 (B)	49 (A)

latin square, ↓	health ↓ age→	$j=1$	$j=2$	$j=3$
	$i=1$	69 (A)	80 (B)	40 (C)
$l=1$	$i=2$	91 (C)	92 (A)	47 (B)
	$i=3$	65 (B)	63 (C)	44 (A)
	$i=1$	68 (A)	89 (C)	62 (B)
$l=2$	$i=2$	80 (B)	95 (A)	68 (C)
	$i=3$	40 (C)	43 (B)	49 (A)

There are (choose one) **one** / **two** / **three** latin squares in this design. Each additional latin square acts as another blocking variable and so reduces the error.

7. *Latin square crossover design.*
Six[1] (6) *patients* are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: dose (1: below 25 mm, 2: 25 to 35 mm, 3: above 35 mm) and frequency (1: once/day, 2: twice/day, 3: thrice/day).

frequency ↓	patient, ↓ dose→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	$m = 1$	69 (A)	80 (B)	40 (C)
	$m = 2$	68 (A)	89 (B)	62 (C)
$i = 2$	$m = 1$	91 (C)	92 (A)	47 (B)
	$m = 2$	80 (C)	95 (A)	68 (B)
$i = 3$	$m = 1$	65 (B)	63 (C)	44 (A)
	$m = 2$	40 (B)	43 (C)	49 (A)

The six (not two!) patients are each measured repeatedly, (three times) for the three drugs (at three different dosages) which appear in a latin square design. In other words, this design combines a repeated measures design with a latin square design and so is called a *latin square crossover design*[2]. In this case, the subject is nested inside (choose one) **frequency** / **dose**.

30.2 Latin Square Model

The latin square model is stated in this section.

Exercise 30.2 (Latin Square Model)
Nine patients are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: age (1: below 25, 2: 25 to 35, 3: above 35) and health (1: poor, 2: fair, 3: good).

health ↓ age→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	69 (A)	80 (B)	40 (C)
$i = 2$	91 (C)	92 (A)	47 (B)
$i = 3$	65 (B)	63 (C)	44 (A)

Using the following latin square model, match appropriately,

$$Y_{ijk} = \mu_{\dots} + \rho_i + \kappa_j + \tau_k + \varepsilon_{ijk},$$

[1]Even though the notation in the tables seem to suggest there is only two patients, there is, in fact, intended to be six different patients in the study. Furthermore, it is not sensible to set up a second arrangement of data, like in previous questions because there six patients, not two.

[2]If two *different* latin squares had been used, the design would have been called a *latin square double crossover design*.

model	example
(a) Y_{ijk}	**(a)** error
(b) $\mu_{\cdots}$	**(b)** health (block, fixed) effect
(c) ρ_i	**(c)** drug (treatment, fixed) effect
(d) κ_j	**(d)** age (block, fixed) effect
(e) τ_k	**(e)** (grand) average of all responses
(f) ε_{ijk}	**(f)** individual response

model	(a)	(b)	(c)	(d)	(e)	(f)
example						

30.3 Analysis of Latin Square Experiments

SAS program: att12-30-3-drugs-latin-inference

Exercise 30.3 (Analysis of Latin Square Experiments: Drug Responses) Nine patients are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: age (1: below 25, 2: 25 to 35, 3: above 35) and health (1: poor, 2: fair, 3: good).

health ↓ age→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	69 (A)	80 (B)	40 (C)
$i = 2$	91 (C)	92 (A)	47 (B)
$i = 3$	65 (B)	63 (C)	44 (A)

1. *Residual Plot Versus Predicted.*
   The residual plot, from the SAS output, indicates
   (choose one) **constant** / **nonconstant** variance.

2. *Normal Probability Plot of Residuals.*
   The normal probability plot, also obtained from the SAS output, indicates
   (choose one) **normal** / **non–normal** residuals.

3. *ANOVA Table*
   The ANOVA table is given by,

Source	*df*	*SS*	*MS*	$E\{MS\}$
Row blocking variable	$r-1$	*SSROW*	*MSROW*	$\sigma^2 + r\frac{\sum \rho_i^2}{r-1}$
Column blocking variable	$r-1$	*SSCOL*	*MSCOL*	$\sigma^2 + r\frac{\sum \kappa_i^2}{r-1}$
Treatment	$r-1$	*SSTR*	*MSTR*	$\sigma^2 + r\frac{\sum \tau_i^2}{r-1}$
Error	$(r-1)(r-2)$	*SSRem*	*MSRem*	σ^2
Total	r^2-1	*SSTO*		

True / **False** where, in this case,

Source	*df*	*SS*	*MS*
Health (rows)	2	592.67	296.33
Age (columns)	2	2194.67	1097.33
Drug (treatments)	2	32.67	16.33
Error	2	216	108
Total	8	3036	

4. *Test drugs at* $\alpha = 0.05$
   $H_0 : \tau_i = 0$ versus
   $H_a :$ at least one $\tau_i \neq 0,\ i = 1, 2, 3.$
   since p–value $P(F > \frac{MSTR}{MSRem} = \frac{16.33}{108} = 0.151; 2, 8) = 0.86 > \alpha = 0.05$
   accept null; that is, drug effect (choose one) **is** / **is not** significant

5. *95% pairwise confidence intervals for drug effect, bonferroni.*
   Calculate all the 95% pairwise confidence intervals for the drug treatment using the Tukey procedure.
   From SAS,
   $\overline{Y}_{..1} = 68.3,\ \overline{Y}_{..2} = 64.0,\ \overline{Y}_{..3} = 64.7$
   $\hat{L}_1 = \overline{Y}_{..1} - \overline{Y}_{..2} = 4.3,$
   $\hat{L}_2 = \overline{Y}_{..1} - \overline{Y}_{..3} = 3.6,$
   $\hat{L}_3 = \overline{Y}_{..2} - \overline{Y}_{..3} = -0.7,$
   $s\{\hat{L}_i\} = \sqrt{MSRem\left(\frac{1}{r} + \frac{1}{r}\right)} = \sqrt{108\left(\frac{1}{3} + \frac{1}{3}\right)} \approx 8.49$
   $T = \frac{1}{\sqrt{2}}q(1 - \alpha; r, (r-1)(r-2)) = \frac{1}{\sqrt{2}}q(0.95; 3, 2) = \frac{8.33}{\sqrt{2}} \approx 5.89$
   and so the CIs are
   $4.3 \pm 8.49(5.89) =$
   (choose one) **(−45.71, 54.31)** / **(−15.12, 32.78)** / **(−21.83, 19.83)**
   $3.6 \pm 8.49(5.89) =$
   (choose one) **(−20.83, 18.83)** / **(−46.41, 53.61)** / **(−21.83, 19.83)**
   $-0.7 \pm 8.49(5.89) =$
   (choose one) **(−20.83, 18.83)** / **(−15.12, 32.78)** / **(−50.71, 49.31)**
   In other words, none of the average responses to the three drugs are different from one another.

30.4 Planning Latin Square Experiments

We look at the efficiency and power of tests in latin square designs.

Exercise 30.4 (Planning Latin Square Experiments: Drug Responses)
Nine patients are subjected to three different drugs (A, B, C). Two blocks, each with

three levels, are used: age (1: below 25, 2: 25 to 35, 3: above 35) and health (1: poor, 2: fair, 3: good).

health ↓ age→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	69 (A)	80 (B)	40 (C)
$i = 2$	91 (C)	92 (A)	47 (B)
$i = 3$	65 (B)	63 (C)	44 (A)

where, recall,

Source	*df*	*SS*	*MS*
Health (rows)	2	592.67	296.33
Age (columns)	2	2194.67	1097.33
Drug (treatments)	2	32.67	16.33
Error	2	216	108
Total	8	3036	

1. *Efficiency measure, latin square compared to CRD*
   Since

$$\begin{aligned}\hat{E}_1 &= \frac{MSROW + MSCOL + (r-1)MSRem}{(r+1)MSRem} \\ &= \frac{296.33 + 1097.33 + (3-1)(108)}{(3+1)(108)} \\ &= \end{aligned}$$

   (circle one) **0.00** / **3.73** / **0.87**,
   which indicates the Latin square design reduces the error variance 3.73–fold, as compared to the comparable completely randomized design (CRD).

2. *Efficiency measure, latin square (column) compared to RBD*
   Since

$$\begin{aligned}\hat{E}_2 &= \frac{MSCOL + (r-1)MSRem}{rMSRem} \\ &= \frac{1097.33 + (3-1)(108)}{3(108)} \\ &= \end{aligned}$$

   (circle one) **0.00** / **0.34** / **4.05**.
   which indicates the Latin square (column alone) design reduces the error variance 4.05–fold, as compared to the comparable randomized block design (RBD).

3. *Efficiency Measure, latin square (row) compared to RBD*
   Since

$$\begin{aligned}\hat{E}_3 &= \frac{MSROW + (r-1)MSRem}{rMSRem} \\ &= \frac{296.33 + (3-1)(108)}{3(108)} \\ &= \end{aligned}$$

   (circle one) **1.58** / **0.34** / **0.87**.
   which indicates the Latin square (row alone) design reduces the error variance 1.58–fold, as compared to the comparable randomized block design (RBD).

4. *Power of F Test.*
   Assume $\sigma = 100$. What is the power of the test for treatment effects if $\tau_1 = 4$, $\tau_2 = 0$ and $\tau_3 = -4$? Since

$$\begin{aligned}\phi &= \frac{1}{\sigma}\sqrt{\sum \tau_k^2} \\ &= \frac{1}{100}\sqrt{(4)^2 + (0)^2 + (-4)^2} \\ &= 0.06\end{aligned}$$

   and $\nu_1 = r - 1 = 3 - 1 = 3$
   $\nu_2 = (r-1)(r-2) = (2)(1) = 2$
   and so, using Table B.11 (p 1356), the power $1 - \beta$ is
   (circle one) **0.00** / **0.11** / **0.87**.
   In other words, the power (where zero (0) is "poor" and one (1) is "excellent") of the test associated with the latin square in this case is
   (choose one) **poor** / **good**.

30.5 Regression Approach to Latin Square Designs

SAS program: att12-30-5-drugs-latin-regression

We use the regression approach to deal with missing observations in latin square designs.

Exercise 30.5 (Regression Approach to Latin Square Designs)
Eight patients (not nine–one observation is missing!) are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: age (1: below 25, 2: 25 to 35, 3: above 35) and health (1: poor, 2: fair, 3: good).

health ↓ age→	$j = 1$	$j = 2$	$j = 3$
$i = 1$	missing (A)	80 (B)	40 (C)
$i = 2$	91 (C)	92 (A)	47 (B)
$i = 3$	65 (B)	63 (C)	44 (A)

1. *Regression Approach, Full Model*
   Using the SAS output, the full model is

$$\begin{aligned} Y_{ijk} = \mu_{...} &+ \rho_1 X_{ijk1} + \rho_2 X_{ijk2} \\ &+ \kappa_1 X_{ijk3} + \kappa_2 X_{ijk4} \\ &+ \tau_1 X_{ijk5} + \tau_2 X_{ijk6} \\ &+ \varepsilon_{ijk} \end{aligned}$$

   where

$$X_{ijk1} = \begin{cases} 1, & \text{if case from row block 1} \\ -1, & \text{if case from row block 3} \\ 0, & \text{otherwise,} \end{cases}$$

   and X_{ijk2} is defined similarly,

$$X_{ijk3} = \begin{cases} 1, & \text{if case from column block 1} \\ -1, & \text{if case from column block 3} \\ 0, & \text{otherwise,} \end{cases}$$

   and X_{ijk4} is defined similarly

$$X_{ij5} = \begin{cases} 1, & \text{if case from treat 1} \\ -1, & \text{if case from treat 3} \\ 0, & \text{otherwise,} \end{cases}$$

   and X_{ijk6} is defined similarly
   and so an estimate of the *full* model is

$$\begin{aligned} \hat{Y} = 68.67 &+ 15.33X_1 + 9.67X_2 \\ &+ 3.33X_3 + 8X_4 \\ &+ 8.67X_5 - 4.67X_6 \end{aligned}$$

   where $SSE(F)$ = (choose one) **0.00** / **0.11** / **54.0**.

2. *Regression Approach, Reduced Model*
   Using the SAS output, the reduced model (assuming there is no drug response effect) is

$$\begin{aligned} Y_{ijk} = \mu_{...} &+ \rho_1 X_{ijk1} + \rho_2 X_{ijk2} \\ &+ \kappa_1 X_{ijk3} + \kappa_2 X_{ijk4} \\ &+ \varepsilon_{ijk} \end{aligned}$$

which has the estimate,

$$\hat{Y} = 66.5 + 11X_1 + 11.83X_2 - X_3 + 10.17X_4$$

where $SSE(R) =$ (choose one) **54.0** / **74.56** / **223.7**.

3. *Regression Approach, Test of Drug Response*
   $H_0 : \tau_i = 0$ versus
   $H_a :$ at least one $\tau_i \neq 0,\ i = 1, 2, 3.$

$$\frac{SSE(R) - SSE(F)}{df_R - df_F} \div \frac{SSE(F)}{df_F} = \frac{223.67 - 54}{3 - 1} \div \frac{54}{1} = 1.57$$

   and so p–value is $P(F > 1.57; 2, 1) \approx$ (choose one) **0.34** / **0.44** / **0.49**.
   since p–value $= 0.49 > \alpha = 0.05$
   accept null; that is, same average responses for different drugs

30.6 Additional Replications with Latin Square Designs

SAS program: att12-30-6-drugs-latin-replications-inference

We look at latin square designs with replications.

Exercise 30.6 (Additional Replications with Latin Square Designs)
Eighteen (18) patients are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: age (1: below 25, 2: 25 to 35, 3: above 35) and health (1: poor, 2: fair, 3: good).

replication, ↓	health ↓ age→	$j = 1$	$j = 2$	$j = 3$
	$i = 1$	69 (A)	80 (B)	40 (C)
$l = 1$	$i = 2$	91 (C)	92 (A)	47 (B)
	$i = 3$	65 (B)	63 (C)	44 (A)
	$i = 1$	68 (A)	89 (B)	62 (C)
$l = 2$	$i = 2$	80 (C)	95 (A)	68 (B)
	$i = 3$	40 (B)	43 (C)	49 (A)

1. *Residual Plot Versus Predicted.*
   The residual plot, from the SAS output, indicates
   (choose one) **constant** / **nonconstant** variance.

2. *Normal Probability Plot of Residuals.*
   The normal probability plot, also obtained from the SAS output, indicates
   (choose one) **normal** / **non–normal** residuals.

3. *ANOVA Table*
   The latin square with replications model is given by

$$Y_{ijkm} = \mu_{...} + \rho_i + \kappa_j + \tau_k + \varepsilon_{ijkm},$$

where the ANOVA table is,

Source	*df*	*SS*	*MS*
Row blocking variable	$r-1$	*SSROW*	*MSROW*
Column blocking variable	$r-1$	*SSCOL*	*MSCOL*
Treatment	$r-1$	*SSTR*	*MSTR*
Error	$n(r-1)(r-2)$	*SSRem*	*MSRem*
Total	nr^2-1	*SSTO*	

True / **False** which, in this case, is

Source	*df*	*SS*	*MS*
Health (rows)	2	2422.33	1211.16
Age (columns)	2	2006.33	100316
Drug (treatments)	2	129.33	64.67
Error	11	1562.5	142.045
Total	17	6120.5	

4. *Test drugs at* $\alpha = 0.05$
   $H_0 : \tau_i = 0$ versus
   $H_a :$ at least one $\tau_i \neq 0,\ i = 1, 2, 3.$
   since p–value $P(F > \frac{MSTR}{MSRem} = \frac{64.67}{142.045} = 0.46; 2, 11) = 0.64 > \alpha = 0.05$
   accept null; that is, drug effect (choose one) **is** / **is not** significant

30.7 Replications in Repeated Measures Designs

SAS program: att12-30-7-drugs-crossover-inference

We look at a crossover design which combines a repeated measures design with a latin square design.

Exercise 30.7 (Replications in Repeated Measures Designs)
Six[3] (6) *patients* are subjected to three different drugs (A, B, C). Two blocks, each with three levels, are used: dose (1: below 25 mm, 2: 25 to 35 mm, 3: above 35 mm) and frequency (1: once/day, 2: twice/day, 3: thrice/day).

[3] Even though the notation in the tables seem to suggest there is only two patients, there is, in fact, intended to be six different patients in the study.

frequency ↓	patient, ↓ dose→	$j=1$	$j=2$	$j=3$
$i=1$	$m=1$	69 (A)	80 (B)	40 (C)
	$m=2$	68 (A)	89 (B)	62 (C)
$i=2$	$m=1$	91 (C)	92 (A)	47 (B)
	$m=2$	80 (C)	95 (A)	68 (B)
$i=3$	$m=1$	65 (B)	63 (C)	44 (A)
	$m=2$	40 (B)	43 (C)	49 (A)

The six (not two!) patients are each measured repeatedly (three times), for the three drugs (at three different dosages) which appear in a latin square design.

1. *Residual Plot Versus Predicted.*
   The residual plot, from the SAS output, indicates
   (choose one) **constant** / **nonconstant** variance.

2. *Normal Probability Plot of Residuals.*
   The normal probability plot, also obtained from the SAS output, indicates
   (choose one) **normal** / **non–normal** residuals.

3. *ANOVA Table*
   The latin square crossover model is given by

$$Y_{ijkm} = \mu_{\dots} + \rho_i + \kappa_j + \tau_k + \eta_{m(i)} + \varepsilon_{ijkm},$$

   where the ANOVA table is,

Source	*df*	*SS*	*MS*	$E\{MS\}$
Patterns (P)	$r-1$	*SSP*	*MSP*	$\sigma^2 + r\sigma_\eta^2 + nr\frac{\sum \rho_i^2}{r-1}$
Order positions (O)	$r-1$	*SSO*	*MSO*	$\sigma^2 + nr\frac{\sum \kappa_i^2}{r-1}$
Treatment (TR)	$r-1$	*SSTR*	*MSTR*	$\sigma^2 + nr\frac{\sum \tau_k^2}{r-1}$
Subjects (S, within patterns)	$r(n-1)$	*SSS*	*MSS*	$\sigma^2 + r\sigma_\eta^2$
Error	$(r-1)(nr-2)$	*SSRem*	*MSRem*	σ^2
Total	nr^2-1	*SSTO*		

   True / **False** which, in this case, is

Source	*df*	*SS*	*MS*
Frequency (patterns, P)	2	2422.33	1211.16
Dose (order, O)	2	2006.33	1003.16
Drug (treatments, TR)	2	129.33	64.67
Patient(frequency) (subjects, S)	3	444.83	148.277
Error	8	1117.67	139.708
Total	17	6120.5	

4. *Test various at* $\alpha = 0.05$
   $H_0 : \tau_i = 0$ versus
   $H_a :$ at least one $\tau_i \neq 0,\ i = 1, 2, 3.$
   since p–value $P(F > \frac{MSTR}{MSRem} = \frac{64.67}{139.708} = 0.46; 2, 8) = 0.65 > \alpha = 0.05$
   accept null; drug effect (choose one) **is** / **is not** significant
   (average drug response same for different drugs)

   $H_0 : \rho_i = 0$ versus
   $H_a :$ at least one $\rho_i \neq 0,\ i = 1, 2, 3.$
   since p–value $P(F > \frac{MSP}{MSS} = \frac{1211.16}{148.277} = 8.17; 2, 3) = 0.06 > \alpha = 0.05$
   accept null; frequency effect (choose one) **is** / **is not** significant
   (average drug response same for different frequency of drug administration)

   $H_0 : \kappa_j = 0$ versus
   $H_a :$ at least one $\kappa_j \neq 0,\ k = 1, 2, 3.$
   since p–value $P(F > \frac{MSO}{MSRem} = \frac{1003.16}{139.708} = 7.18; 2, 8) = 0.02 < \alpha = 0.05$
   reject null; dose effect (choose one) **is** / **is not** significant
   (average drug response different for different drug doses)