Multisample inference - del 2 (Rosner,12.5 - 12.7)

Stian Lydersen

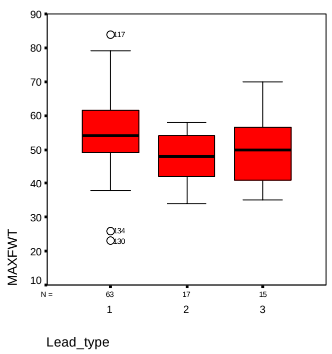
Innhold

- 12.5.2: Sammenheng mellom enveis ANOVA og multippel lineær regresjon: Indikatorvariable
- 12.5.3 samt Vickers & Altman (BMJ Nov 2001): Kovariansanalyse (ANCOVA)
- 12.6: Toveis ANOVA og interaksjon
- 12.7: Kruskall-Wallis test
- Altman 12.3.5: Friedmans test

Data “Effect of Lead Exposure …” (Eks. i Rosner Kap. 12.5 mm)

- Les inn “lead.xls” fra “Rosnerdata”
- MAXFWT = MAX(fwt_l, fwt_r)
- Group er variabelen “lead_type”
- Merk at 99 betyr MISSING
- Fjern de 4 cases med id 149, 210, 212, 312. (Dette er outliers som ble identifisert i Section 8.9, Examples 8.25, 8.26)
- Datafilen finnes på hjemmesiden til faget KLMED 8005.

Lead_type	Blood-lead level in the child	GROUP
1	Normal (<40 µg/100ml) in both 1972 and 1973	Control
2	Elevated (≥40 µg/100ml) in 1973	Currently exposed
3	Elevated in 1972 and normal in 1973	Previously exposed



Rosner, Table 12.7 og 12.8 (12.5 og 12.6 i 5th edition)

Report

MAXFWT

Lead_type	N	Mean	Std. Deviation	Minimum	Maximum
1	63	55,10	10,935	23	84
2	17	47,59	7,080	34	58
3	15	49,40	10,197	35	70
Total	95	52,85	10,638	23	84

ANOVA

MAXFWT

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	966,791	2	483,395	4,598	,012
Within Groups	9671,146	92	105,121		
Total	10637,937	94			

Multippel regresjon som alternativ til enveis ANOVA

En kategorisk variabel C med k nivåer {1, 2, …, k} representeres med k-1 dummy variable (indikatorvariable):

x_1 = 1 (0) hvis C=2 (≠2)
x_2 = 1 (0) hvis C=3 (≠3)
…
x_{k-1} = 1 (0) hvis C=k (≠k)

Referansegruppe (her k=0) velger du selv.

Kan gjøres ”automatisk” i SPSS:
General Linear Model -> Univariate
Legg inn kategorivariablene som ”Fixed factor”

Koding av indikatorvariable

C	x_1	x_2	…	x_{k-1}
1	0	0	…	0
2	1	0	…	0
3	0	1	…	0
…	…	…		…
k	0	0	…	1

Regresjonsmodell:
$y = \alpha + \beta_1 GRP2 + \beta_2 GRP3 + e$

ANOVA[b]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	966,791	2	483,395	4,598	,012[a]
	Residual	9671,146	92	105,121		
	Total	10637,937	94			

a. Predictors: (Constant), GRP3, GRP2
b. Dependent Variable: MAXFWT

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	55,095	1,292		42,652	,000
	GRP2	-7,507	2,802	-,272	-2,679	,009
	GRP3	-5,695	2,946	-,196	-1,933	,056

a. Dependent Variable: MAXFWT

Enveis ANCOVA

- “ANOVA” med justering for andre kovariater
- Fordeler:
  - Unngå skjevheter pga konfundering
  - Mer presis estimering (hypotesetesting)

Eksempel 12.16:

$y = \alpha + \beta_1 GRP2 + \beta_2 GRP3 + \beta_3 age + \beta_4 sex + e$

SPSS Regression -> Linear

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	33,958	3,130		10,851	,000
	GRP2	-5,278	1,974	-,191	-2,674	,009
	GRP3	-4,927	2,061	-,170	-2,391	,019
	AGE	2,449E-02	,002	,705	9,919	,000
	SEX	-2,408	1,515	-,112	-1,589	,116

a. Dependent Variable: MAXFWT

SPSS General Linear Model -> Univariate

Tests of Between-Subjects Effects

Dependent Variable: MAXFWT

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	6017,809[a]	4	1504,452	29,307	,000	,566
Intercept	5157,872	1	5157,872	100,475	,000	,527
LEAD_TYP	549,784	2	274,892	5,355	,006	,106
AGE	5050,289	1	5050,289	98,380	,000	,522
SEX	129,633	1	129,633	2,525	,116	,027
Error	4620,128	90	51,335			
Total	276011,000	95				
Corrected Total	10637,937	94				

a. R Squared = ,566 (Adjusted R Squared = ,546)

SPSS General Linear Model -> Univariate (forts.)

Parameter Estimates

Dependent Variable: MAXFWT

Parameter	B	Std. Error	t	Sig.	95% Confidence Interval		Partial Eta Squared
					Lower Bound	Upper Bound	
Intercept	29,032	3,511	8,270	,000	22,057	36,006	,432
[LEAD_TYP=1]	4,927	2,061	2,391	,019	,833	9,021	,060
[LEAD_TYP=2]	-,351	2,548	-,138	,891	-5,413	4,710	,000
[LEAD_TYP=3]	0[a]	,	,	,	,	,	,
AGE	2,449E-02	,002	9,919	,000	1,959E-02	2,940E-02	,522
SEX	-2,408	1,515	-1,589	,116	-5,418	,602	,027

a. This parameter is set to zero because it is redundant.

Merk: SPSS default er siste nivå (her lead_typ = 3) som referanse

13

Pocock, S. J. & al:
Subgroup analysis, covariate adjustment and baseline comparison in clinical trial reporting: current practice and problems.
Statistics in medicine 2002; **21**: 2917-2930.

p 2927:
"Overall, what matters is to adjust for the appropriate covariates (that is, the strong predictors of outcome) and to make one's statistical policy for covariate adjustment completely objective. …"

14

God artikkel om ANCOVA:
Vickers, A. J. and Altman, D. G.:
Statistics Notes: Analysing controlled trials with baseline and follow up measurements
BMJ, Nov 2001; 323: 1123 - 1124

Eksempel på beskrivelse i "Methods":
"To adjust for baseline scores, we used analysis of covariance to compare outcome between the two groups."

15

Sluttverdi eller endring som outcome? Inkludere baseline verdi i analysen?

Vickers, A J and Altman, D G:
Analysing controlled trials with baseline and follow up measurements
BMJ, vol 323, 10 nov 2001, 1123-1124.

16

Table from Vickers and Altman

17

Alternative analyses

- Not including baseline
  - Follow up score
  - Change score
- Including baseline
  - Follow up score (ANCOVA)
  - Change score: Not correct. Change is usually negatively correlated with baseline

18

Analysis not including baseline

- Follow up score:
  - Most significant if low correlation with baseline
- Change score:
  - Most significant if baseline and follow up are highly correlated

19

Effect of baseline score if not included

- If, by chance, worse baseline scores in treatment group:
  - Follow up score analysis underestimates effect
  - Change score analysis overestimates effect
- If average baseline in the groups are equal
  - Unbiased effect estimate in both analyses, but low power (wide confidence intervals)

20

ANCOVA
(Actually regression analysis)

Follow up score
= constant + a×baseline score + b×group
=24.0 + 0.71×baseline score + 12.7×group

21

Figure from Vickers and Altman

22

12.6: Toveis variansanalyse. Eksempel

Table 12.14 (12.13 in 5th ed):
Mean systolic blood pressure by dietary group and sex

Dietary group		Male	Female
SV	mean	109.9	102.6
	n	138	88
LV	mean	115.5	105.2
	n	26	37
Normal	mean	128.3	119.6
	n	240	220

23

Toveis variansanalyse

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

hvor

y_{ijk} er resultat for k'te person i i'te diettgruppe og j'te kjønn
μ er en konstant
α_i er effekt av rad i (gruppe i)
β_j er effekt av kolonne j (kjønn j)
γ_{ij} er samspill (interaction) mellom gruppe i og kjønn j
$e_{ijk} \sim N(0, \sigma^2)$ representerer variasjon innen cellen (rad og kolonne)

24

Fremgangsmåte:

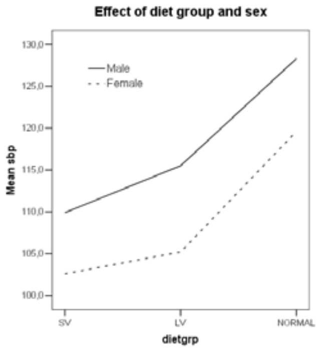
Test først samspillet, dvs H_0: $\gamma_{ij}=0$ for alle i,j.

Hvis samspillet er signifikant, har både rad og kolonne effekt

Hvis samspillet ikke er signifikant brukes modell uten samspill:
$y_{ijk} = \mu + \alpha_i + \beta_j + e_{ijk}$
Test H_0: $\alpha_i=0$ for alle i og/eller $\beta_j = 0$ for alle j

(Rosner gjør bare det siste!)

25



Hvis linjene er (tilnærmet) parallelle, er det ikke samspill

26

Samspill betyr:
Effekt av rad (diett) er forskjellig i forskjellige kolonner (kjønn)

Samspill betyr ikke:
Hvorvidt rad og kolonne er assosiert (f.eks korrellert)

27

Toveis ANCOVA

Eksempel 12.22 (12.19 i 5th ed):

x_1 = 1 if diet group 2
x_2 = 1 if diet group 3
"sex" has only two values (groups).

$y = \alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 \text{sex} + \beta_4 \text{age} + \beta_5 \text{weight} + e$

28

Sammenlikning mellom k grupper:

	Normalfordelte data	**Ikke normalfordelt**
k = 2	To-utvalgs t-test 1)	Wilcoxon-Mann-Whitney's test
k > 2	enveis ANOVA 1)	Kruskall-Wallis' test

1) Alternativt multippel lineær regresjon med indikatorvariable for gruppene. Kan også brukes ved justering for kovariater (f.eks alder, kjønn).

29

Table 12.17 (12.16 in 5^{th} ed):
Ocular anti.inflammatory effects of 4 drugs on lid closure

Rabbit no	Indomethicin	Aspirin	Piroxicam	BW775C
	Score	Score	Score	Score
1	+2	+1	+3	+1
2	+3	+3	+1	0
3	+3	+1	+2	0
4	+3	+2	+1	0
5	+3	+2	+3	0
6	0	+3	+3	-1

Note: There are 6x4 = 24 rabbits!

30

Table 12.18 (12.17 in 5th ed). Assigment of ranks

Lid-closure score	Frequency	Range of ranks	Average rank
-1	1	1	1.0
0	5	2 – 6	4.0
1	5	7 – 11	9.0
2	4	12 – 15	13.5
3	9	16 – 24	20.0

31

Table 12.17 (12.16 in 5th ed):
Ocular anti.inflammatory effects of 4 drugs on lid closure

Rabbit no	Indomethicin		Aspirin		Piroxicam		BW775C	
	Score	Rank	Score	Rank	Score	Rank	Score	Rank
1	+2	13.5	+1	9.0	+3	20.0	+1	9.0
2	+3	20.0	+3	20.0	+1	9.0	0	4.0
3	+3	20.0	+1	9.0	+2	13.5	0	4.0
4	+3	20.0	+2	13.5	+1	9.0	0	4.0
5	+3	20.0	+2	13.5	+3	20.0	0	4.0
6	0	4.0	+3	20.0	+3	20.0	-1	1.0

32

Kruskall-Wallis' test:

k grupper, gruppe nr i har n_i observasjoner og rangsum R_i . $N = \sum_{i=1}^{k} n_i$.

$$H^* = \frac{12}{N(N+1)} \sum_{i=1}^{k} n_i [R_i / n_i - \underbrace{(N+1)/2}_{E(R_i/n_i) \text{ under } H_0}]^2 = \underbrace{\frac{12}{N(N+1)} \sum_{i=1}^{k} \frac{R_i^2}{n_i} - 3(N+1)}_{\text{Lettere å regne ut}}$$

$$H = \frac{H^*}{1 - \frac{\sum_{j=1}^{g} (t_j^3 - t_j)}{N^3 - N}}$$

hvor t_j er antall sammenfallende observasjoner i klynge nr j

er tilnærmet χ^2_{k-1} under H_0.

33

SPSS:
Nonparametric tests -> k independent samples

Ranks

	DRUG	N	Mean Rank
LIDSCORE	Indomechitin	6	16,25
	Aspirin	6	14,17
	Piroxicam	6	15,25
	BW755C	6	4,33
	Total	24	

Test Statistics[a,b]

	LIDSCORE
Chi-Square	11,804
df	3
Asymp. Sig.	,008
Exact Sig.	,003
Point Probability	,000

a. Kruskal Wallis Test
b. Grouping Variable: DRUG

34

12.7. Multiple sammenlikninger (Dunn prosedyren)

Regn ut

$$z = \frac{\overline{R}_i - \overline{R}_j}{\sqrt{\frac{N(N+1)}{12} \times \left(\frac{1}{n_i} + \frac{1}{n_j} \right)}}$$

Forkast H_0 hvis $|z| > z_{1-\alpha^*}$ hvor $\alpha^* = \frac{\alpha}{k(k-1)}$

Merk at dette tilsvarer Bonferroni korreksjon

35

Eks. (Forts)

Ranks

	DRUG	N	Mean Rank
LIDSCORE	Indomechitin	6	16,25
	Aspirin	6	14,17
	Piroxicam	6	15,25
	BW755C	6	4,33
	Total	24	

$z_{12} = 0.51$, $z_{13} = 0.24$, $z_{14} = 2.92$, $z_{23} = -0.27$, $z_{24} = 2.41$, $z_{34} = 2.67$

$\alpha^* = \frac{0.05}{4(4-1)} = 0.0042$, $z_{1-0.0042} = 2.64$

Altså:
Gruppe 1 og 4 er forskjellige
Gruppe 3 og 4 er forskjellige

36

Friedman's to-veis ANOVA (Altman, 12.3.5)

- Krever ikke normalfordeling
- n subjekter og k grupper. Én observasjon per celle (subjekt og gruppe). Få eller ingen sammenfallende observasjoner.
- H_0 (H_1) : Det er ikke (er) forskjell på gruppene

37

Table 12.9 Immersion suit leakage (g) during simulated helicopter underwater escape (Light *et al.*, 1987)
From Altman (1991)

	Suit type			
Subject	A	B	C	D
1	308	132	454	64
2	102	526	0	28
3	182	134	96	30
4	268	324	264	90
5	166	228	134	34
6	332	296	458	6
7	198	350	200	90
8	28	274	16	24
Mean	198	283	302	45.7
SD	103	127	179	31.6

38

Table 12.10. Ranks of the data in Table 12.9.
From Altman (1991)

	Suit type			
Subject	A	B	C	D
1	3	2	4	1
2	3	4	1	2
3	4	3	2	1
4	3	4	2	1
5	3	4	2	1
6	3	2	4	1
7	2	4	3	1
8	3	4	1	2
Total (R)	24	27	19	10
Mean rank	3.00	3.38	2.38	1.25

39

Friedman's test:

$$H = \frac{12}{nk(k+1)}\sum_{i=1}^{k}[R_i - \underbrace{n(k+1)/2}_{E(R_i)\text{ under }H_0}]^2 = \underbrace{\frac{12}{nk(k+1)}\sum_{i=1}^{k} R_i^2 - 3n(k+1)}_{\text{Lettere å regne ut}}$$

er tilnærmet χ^2_{k-1} under H_0.
(R_i er rangsum i gruppe i)

Eksempel:

$$H = \frac{12}{8\times4\times5}[24^2+27^2+19^2+10^2]-3\times8\times5=12.45$$

p-verdi ≈ P(χ^2_{4-1} ≥ 12.45) = 0.006

40

Friedman's test i SPSS:

- Et case pr subjekt, en variabel pr gruppe
- Analyse -> Nonparametric tests -> k related samples
- Opsjonen "Exact" gir p-verdien eksakt ("Exact Sig.") i tillegg til kji-kvadratfordeligens tilnærming ("Asymp. Sig")

41

Friedman Test

Ranks

	Mean Rank
A	3,00
B	3,38
C	2,38
D	1,25

Test Statistics[a]

N	8
Chi-Square	12,450
df	3
Asymp. Sig.	,006
Exact Sig.	,003
Point Probability	,000

a. Friedman Test

42

Hvilke grupper er forskjellige?

- Friedman's test forteller om minst to grupper er forskjellige. (I eksempelet har D åpenbart lavere verdier)
- Par av grupper kan sammenliknes vha Wilkoxons test for matchede par. Juster for multiple sammenlikninger.
- Friedman's test for 2 grupper tilsvarer tegn-testen!

43