

Lecture L11b: Analysis of clustered data (VER Ch. 20)

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Learning objectives:

- Understand the concept of clustering in risk factor analysis
- Understand common data structures associated with clustering
- Understand the effect of clustering when using continuous and binary data
- Use Stata to analyze clustered data

Wednesday April 1st :

- Quiz 9 – Cox models
-

Clusters

- observations that share some feature(s) in common
 - ★ not considered by the predictors of the model
- derived from data structure
- observations within a cluster “more alike” (usually)
 - ★ due to common features
- observations within a cluster “less alike” (occasionally)
 - ★ competition for feed

Sources of clustering

- common environment
 - ★ eg. fish in a pen, cows in a herd, child in a school
 - ★ same correlation among all pairs
 - ➔ Daisy and Nelly has same correlation as Daisy and Jessie from the same farm
 - ★ multiple levels
 - ➔ region -> herd -> cow-> lactation

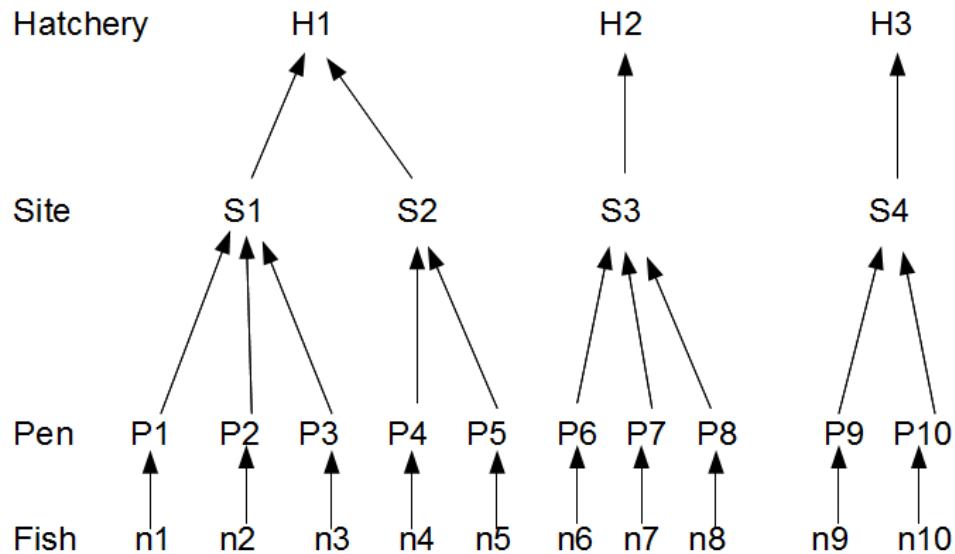
 - ➔ hierarchical or multilevel structure

- spatial clustering
 - ★ dependence depends on distance among units
 - ★ topographical features??
- repeated measurements (temporal clustering)
 - ★ dependence depends on separation in time between observations
 - milk production more highly correlated with preceding day's production than production from 1 month ago
 - ★ data from 3 cows - 1st 6 monthly tests of the lactation
 - dim = days in milk at time of test
 - milk = daily milk production (energy corrected)

Herd	Cow		Test Number					
			1	2	3	4	5	6
1	5	dim	11	39	67	102	130	165
		milk	25.12	19.92	19.13	20.38	18.21	14.64
1	12	dim	18	46	74	109	137	172
		milk	18.13	21.28	16.64	16.4	15.63	10.37
1	14	dim	23	58	86	121	149	177
		milk	18.84	18.81	17.1	13.47	11.29	10.46

Hierarchical vs cross-classified structures

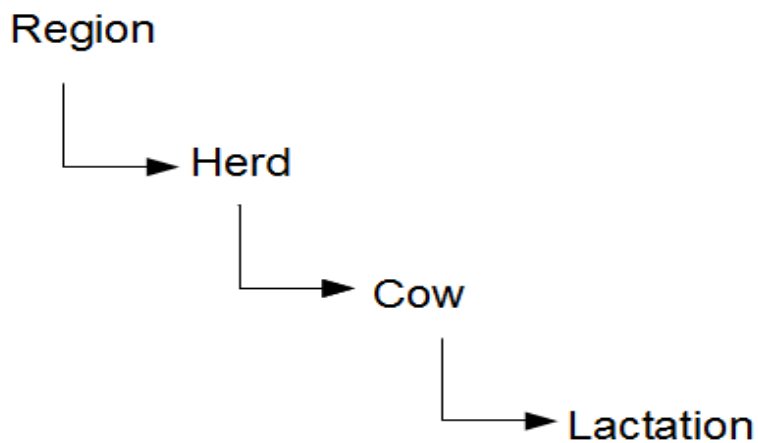
- (a) Hierarchical structure
 - ★ requires that every site receives fish from one hatchery
 - ★ requires that every pen is located within one site



- (b) Cross-classified structure
 - ➔ different pens at the same site receive fish from different hatcheries

Clustering of outcomes vs predictors

- Clustering of outcome
 - ★ violates standard assumption of independence
 - ➔ ordinary linear or logistic models are invalid
 - ★ identify levels with greatest variation
 - ➔ potential room for improvement
 - ★ outcomes usually at lowest level
- Clustering of the predictors
 - ★ predictors at various levels
 - ★ sample size?



Effects of clustering

- If you ignore clustering – general
 - ★ SE of parameter estimates usually too small
 - much too small for group levels predictors
 - may be too large for individual level predictors
 - ★ assign unreasonable large weights to large groups
 - ★ parameter estimates “asymptotically” unbiased
 - limited sample size estimates may be biased (discrete)
 - ★ discrete data models (eg. logistic regression)
 - estimates are “marginal estimates” instead of “cluster specific” estimates (described later)
 - eg. often get different parameter estimates if do/don't control for clustering

Effect of clustering – continuous data (Example 20.2)

- Data structure

- ★ 100 herds

- 50 small herds (avg. 50 cows)

- 50 large herds (avg. 200 cows)

- ★ outcome = milk production

- varies between herds

- herd mean = 30 kg/day, SD = 7 kg/day

- cow level SD = 8 kg/day

- ★ predictor = X (herd or cow level factor)

- true effect = +5 kg/day

X → Y

- herd:

- TMR vs component

- cow:

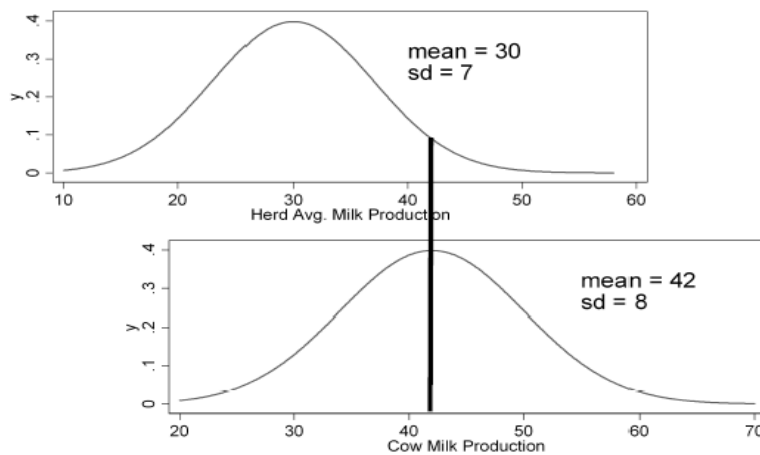
- rBST

- milk production

- $\mu = 30$ kg/day

- $\sigma_h = 7$ kg/day

- $\sigma_i = 8$ kg/day



● Scenario 1- X herd level variable

★ ignoring clustering

```
. reg milk X
```

```
Number of obs = 11626 - Root MSE = 10.733
```

```
...
```

milk	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
X	3.55661	.199534	17.82	0.000	3.16549 3.94773
_cons	30.0215	.1457715	205.95	0.000	29.73576 30.30723

★ accounting for cluster

```
. mixed milk X || herd: , reml stddev
```

```
Mixed-effects REML regression
```

```
Group variable: herd
```

```
Number of obs = 11626
```

```
Number of groups = 100
```

```
Obs per group: min = 20
```

```
avg = 116.3
```

```
max = 311
```

```
Log restricted-likelihood = -40902.479
```

```
Wald chi2(1) = 6.44
```

```
Prob > chi2 = 0.0112
```

milk	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
X	3.796004	1.495943	2.54	0.011	.864009 6.727999
_cons	31.13696	1.058717	29.41	0.000	29.06191 33.21201

Random-effects Parameters	Estimate	Std. Err.	[95% Conf. Interval]
herd: Identity			
sd(_cons)	7.410465	.5396842	6.424728 8.547442
sd(Residual)	8.012545	.0527739	7.909774 8.11665

```
Likelihood ratio test vs. linear regression: chibar2(01) = 6374.40 Prob >= chibar2 = 0.0000
```

★ data collapsed to herd level

```
. collapse (mean) milk X, by(herd)
```

```
. reg milk X
```

```
.....
```

```
Number of obs = 100 - Root MSE = 7.48
```

milk	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
X	3.778772	1.497421	2.52	0.013	.8071885 6.750356
_cons	31.16586	1.058837	29.43	0.000	29.06463 33.26708

- Scenario 2: X is a cow level variable

- ★ X has a prevalence of 0.5 in all herds (eg. clinical trial)

- ★ ignoring clustering

```
. reg milk X
```

Source	SS	df	MS			
Model	72138.7619	1	72138.7619	Number of obs =	11626	
Residual	1341880.62	11624	115.440522	F(1, 11624) =	624.90	
Total	1414019.39	11625	121.636076	Prob > F =	0.0000	
				R-squared =	0.0510	
				Adj R-squared =	0.0509	
				Root MSE =	10.744	

milk	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
X	4.982006	.1992962	25.00	0.000	4.591352	5.37266
_cons	29.25664	.1412627	207.11	0.000	28.97974	29.53354

- ★ accounting for clustering

```
. mixed milk X || herd:, reml stddev
```

```
Mixed-effects REML regression          Number of obs      =      11626
Group variable: herd                   Number of groups   =         100

Obs per group: min =          20
                avg =        116.3
                max =          311

Log restricted-likelihood = -40947.175   Wald chi2(1)       =      1108.56
                                          Prob > chi2        =         0.0000
```

milk	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
X	4.968194	.1492174	33.30	0.000	4.675733	5.260655
_cons	30.64647	.7281276	42.09	0.000	29.21936	32.07357

Random-effects Parameters	Estimate	Std. Err.	[95% Conf. Interval]	
herd: Identity				
sd(_cons)	7.170209	.5201795	6.219843	8.265787
sd(Residual)	8.044296	.0529852	7.941114	8.148818

```
LR test vs. linear regression: chibar2(01) = 6310.00 Prob >= chibar2 = 0.0000
```

- Summary herd and cow level analyses

Dataset	Parameter	Linear regression		Mixed model		Herd average	
		β	SE	β	SE	β	SE
X herd level	X	3.56	0.20	3.80	1.50	3.78	1.50
	intercept	30.02	0.15	31.14	1.06	31.17	1.06
X cow level	X	4.98	0.20	4.97	0.15		
	intercept	29.26	0.14	30.65	0.73		

- Scenario 1 - X is a herd level variable
 - ★ ignoring clustering produces SE much lower that they should be
 - ★ herd averages very similar estimates as mixed model
- Scenario 2 - X is a cow level variable
 - ★ mixed model estimate close to the true and more precise
 - ★ intercept underestimate SE if clustering is ignored

Effect of clustering – discrete data (Example 20.3)

- Effect of X on probability of disease (outcome)
 - ★ prevalence of X = 0.50
 - ➔ herd level: 50% herds with X=1(0) (all cows within each herd with the same level of the predictor)
 - ➔ cow level: 50% cows X=1(0) within herd
 - ★ $OR_x = 2$ (or $\ln(2) = 0.693$ on logistic scale)
 - ★ disease non-exposed $p = 0.2$ (or $\ln(0.2/0.8) = -1.4$ on logistic scale)
 - ★ herd level effects varied (on logistic scale) with $var = 1$
- Scenario 1 – X is a herd level variable (Ex. 20.3)

★ ignoring clustering

```
. logit Y X
```

Y	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
X	.5287317	.0423191	12.49	0.000	.4457877	.6116757
_cons	-1.241768	.0325699	-38.13	0.000	-1.305604	-1.177932

★ accounting for clustering

```
. melogit Y X || herd:
```

Y	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
X	.6199967	.2037578	3.04	0.002	.2206389	1.019355
_cons	-1.305448	.1454551	-8.97	0.000	-1.590534	-1.020361
herd						
var(_cons)	.9417563	.1493109			.6902154	1.284968

Likelihood ratio test vs. logistic model: $\chi^2(1) = 1499.38$ Prob >= $\chi^2 = 0.0000$

- Summary herd and cow level analyses

Dataset	Parameter	Logistic regression		Logistic mixed model	
		β	SE	β	SE
X herd level	X	0.53	0.04	0.62	0.20
	intercept	-1.24	0.03	-1.31	0.15
X cow level	X	0.59	0.04	0.70	0.05
	intercept	-1.25	0.03	-1.36	0.11

- In general, ignoring clustering underestimates SE
- Can't compare estimates between log. reg. and mixed model (next lecture)

Variance inflation as a result of clustering

- Group level predictor (outcome of interest is mean value for groups)
- Variance of group mean affected by:
 - ★ ICC (intra-class correlation coefficient - ρ)
 - ➔ measure of similarity between observations within a cluster
 - ★ group size
- Variance of group means is:

$$Var(\bar{y}) = \frac{\sigma^2}{m} * VIF$$

★ where

- ➔ m = group size ;
- ➔ σ^2 = within-group $\text{var}(y_i)$, and
- ➔ $VIF = [1 + (m-1)*\rho]$ = Variance Inflation Factor

★ $ICC(\rho) = 0 \rightarrow Var(\bar{y}) = \frac{\sigma^2}{m}$

→ independent observations – all observations

★ $ICC(\rho) = 1 \rightarrow Var(\bar{y}) = \frac{\sigma^2}{m} * m$

→ complete correlation – one observation

ICC	m	VIF	Comments
0	20	1	no within group correlation = no VIF added to Var(y)
1	20	20	complete within group correlation => VIF = m
0.1	6	1.5	low ICC and moderate group size had similar impact as
0.5	2	1.5	high ICC and small group
0.1	101	11	very large group size, even with low ICC has a very big impact

- VIF can be used to adjust sample size estimates for clustering (VER Ch. 2.11.6)

★ $n' = n * [1 + (m - 1) * \rho]$

★ effective sample size will be = m/VIF

→ 20 cows per herd and high ICC (e.g. 1)

→ effective sample size = $20/20 = 1$