



# Linear Regression

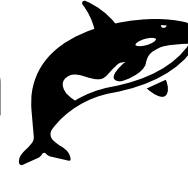
## Module III: Deep Dive

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University of North Dakota

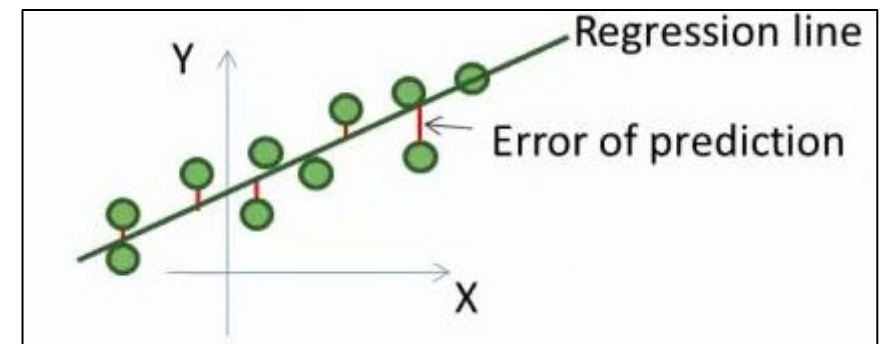
# Introduction



- Previously:
  - Covered a broad overview
  - Looked at more detail
  - Ran through examples
- This time: looked at more advanced linear regression methods
  - Generalized Linear Mixed Model
  - Longitudinal Analysis
  - Structural Equation Modeling

# Reviewing the Basics

- Linear regression: modeling the relationship between a response variable and one or more predictor variables
  - Structure->simple, multiple, multivariate
  - Predictor variables->polynomial, fixed/random, nested
  - Response variables->Gaussian, Logistic, Poisson, etc.
  - Other considerations
- Process of ordinary least squares
- Need to consider assumptions and model fit
- Lots of ways to run a regression



# Topics Covered

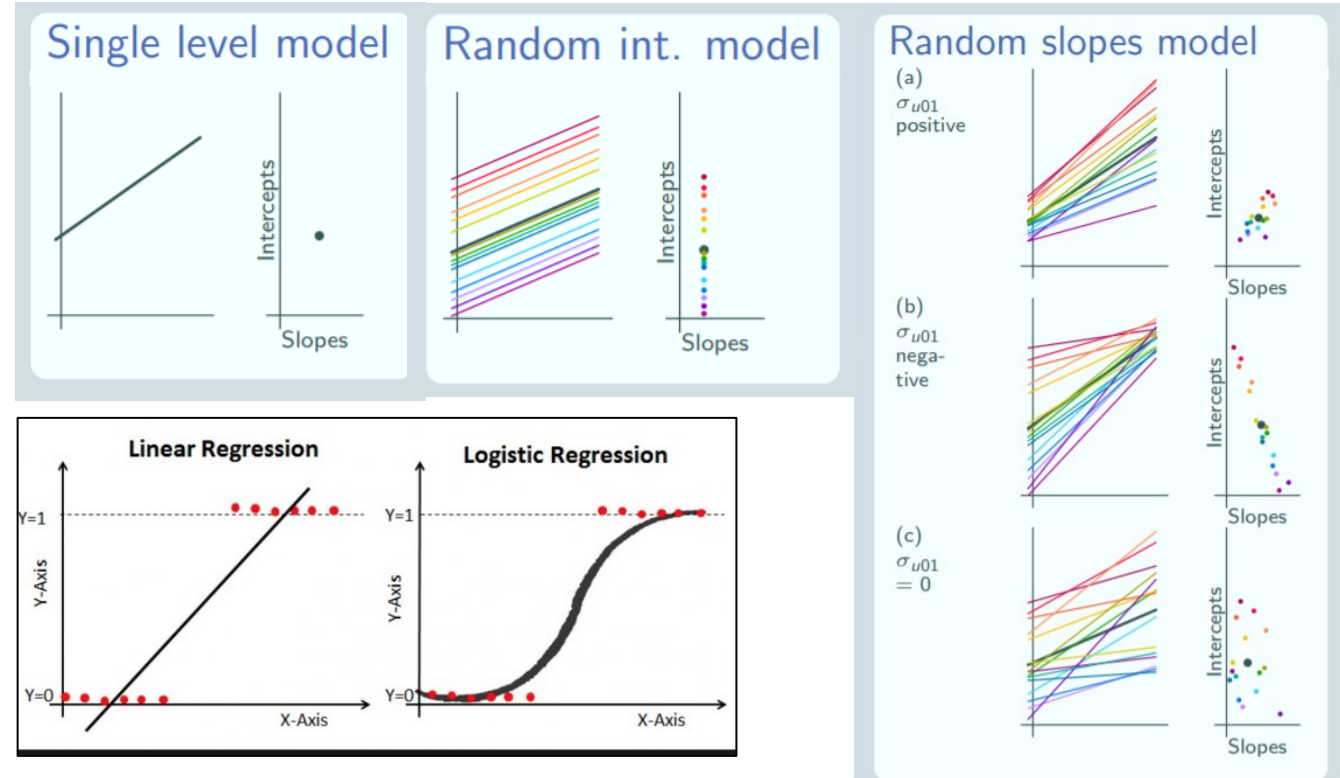
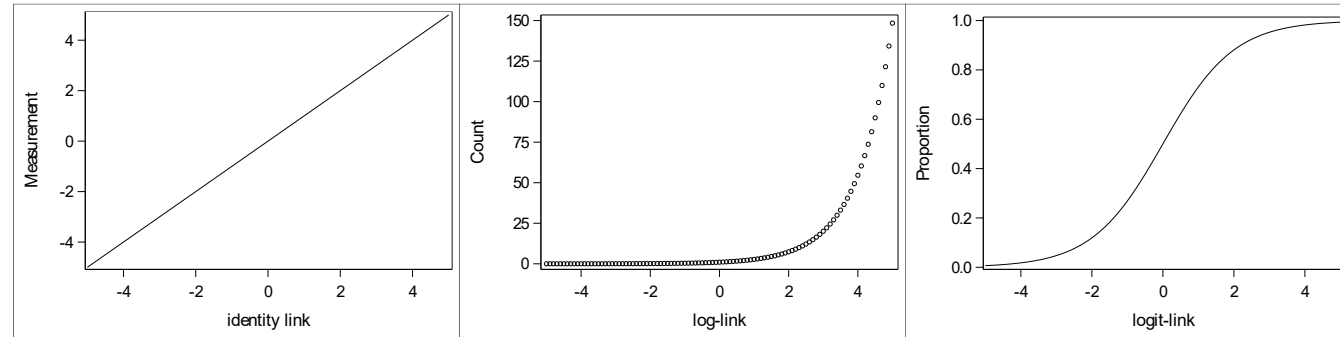
- Generalized Linear Mixed Model
  - Software: SAS Studio
- Longitudinal Analysis
  - Software: R
- Structural Equation Modeling
  - Software: STATA



# Generalized Linear Mixed Models

## Descriptions

- A Generalized Linear Mixed Model is combination of a Generalized Linear Model and a Linear Mixed Model
  - Generalized -> accommodates non-normal distributions
  - Mixed -> allows for random effects
- Key differences in generalized linear mixed model and linear model:
  - Method of estimation: Ordinary Least Squares vs. Maximum Likelihood (iteratively maximize likelihood of parameters given data)
  - Distributions: Normal distribution vs. Others
  - Model scale: GLMMs link expected values to model scale with link
- Random Intercepts/ Random Slopes:





# Generalized Linear Mixed Models

## Formats

### **Basic (Random Intercepts):**

```
PROC GLIMMIX data=dataset;  
    class TREATMENT RANDOM;  
    model RESPONSE= TREATMENT;  
    random intercept /subject=RANDOM;
```

```
PROC GLIMMIX data=dataset;  
    class RANDOM;  
    model RESPONSE= TREATMENT;  
    random intercept /subject=RANDOM;
```

```
PROC GLIMMIX data=dataset;  
    class RANDOM;  
    model RESPONSE= TREATMENT;  
    random RANDOM;
```

### **Nested:**

```
PROC GLIMMIX data=dataset;  
    class TEACHINGSTYLE STATE SCHOOL;  
    model RESPONSE = TEACHINGSTYLE;  
    random STATE SCHOOL(STATE);
```

### **Random Effects Only;**

```
PROC GLIMMIX data=dataset;  
    class TREE BRANCH LEAF;  
    model RESPONSE = ;  
    random TREE BRANCH(TREE) LEAF(BRANCH TREE);
```

### **Random Slopes:**

```
PROC GLIMMIX data=dataset;  
    class RANDOM;  
    model RESPONSE = TREATMENT;  
    random intercept TREATMENT/subject=RANDOM;
```

# Generalized Linear Mixed Models

## Examples

Multicenter<sup>1</sup>

NPK

RC<sup>2</sup>

Wings

```
1  
2 *EXAMPLE 1: Basic GLMM with Categorical Treatment;  
3 DATA multicenter;  
4   input center group$ n SideEffect @@;  
5   datalines;  
6 1 A 32 14 1 B 33 18 2 A 30 4 2 B 28 8  
7 3 A 23 14 3 B 24 9 4 A 22 7 4 B 22 10  
8 5 A 20 6 5 B 21 12 6 A 19 1 6 B 20 3  
9 7 A 17 2 7 B 17 6 8 A 16 7 8 B 15 9  
10 9 A 13 1 9 B 14 5 10 A 13 3 10 B 13 1  
11 11 A 11 1 11 B 12 2 12 A 10 1 12 B 9 0  
12 13 A 9 2 13 B 6 14 A 8 1 14 B 8 1  
13 15 A 7 1 15 B 8 0  
14 ;  
15  
16 PROC PRINT data=multicenter;  
17  
18 DATA multicenter; set multicenter;  
19   Prop_SideEffect = SideEffect/n;  
20  
21 PROC SGPLOT data=multicenter;  
22   vbox Prop_SideEffect /group=group;  
23  
24 PROC SGPLOT data=multicenter;  
25   vbox Prop_SideEffect/ group=center;  
26  
27 PROC GLIMMIX data=multicenter;  
28   class group;  
29   model SideEffect/n = group /solution;  
30  
31 PROC GLIMMIX data=multicenter;  
32   class center group;  
33   model SideEffect/n = group / solution;  
34   random center;  
35  
36 PROC GLIMMIX data=multicenter; *same as above;  
37   class center group;  
38   model SideEffect/n = group / solution;  
39   random intercept / subject=center; *random intercept;  
40   lsmeans group / ilink cl;  
41   ods output LSMeans=lsml;  
42  
43
```

<sup>1</sup><https://support.sas.com/resources/papers/proceedings/proceedings/sugi30/196-30.pdf>

<sup>2</sup><https://v8doc.sas.com/sashtml/stat/chap41/sect33.htm>

# Generalized Linear Mixed Models

## Examples

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10 9 A 13 1 9 B 14 5 10 A 13 3 10 B 13 1  
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# Assessment 1

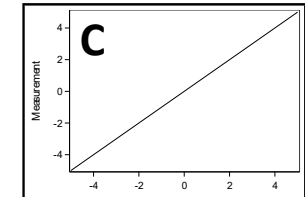
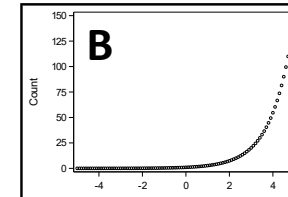
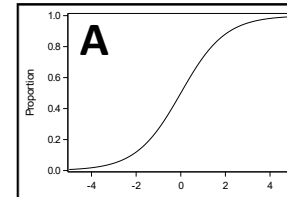


1. You want to run PROC GLIMMIX to model a medical outcome (Med) as a function of a categorical treatment (Treat) with the hospital (Hosp) as a random effect. How would you set up the following SAS code?

```
PROC GLIMMIX data=dataset;
CLASS _____;
MODEL _____ = _____;
RANDOM intercept /subject=_____;
```

2. Match the following distributions to their appropriate link function (A, B, or C).

- 1) Poisson    2) Negative Binomial    3) Binary    4) Normal



3. Which of the following are likely random effects?

Treatment, School, Ethnicity, Temperature, Block, Color, Chemical concentration, Site

4. Below are tables from a GLIMMIX procedure. Is the fixed effect significant, did the random effect affect the results, and is the model a good fit?

Covariance Parameter Estimates			
Cov Parm	Subject	Estimate	Standard Error
Intercept	colony	0.1144	0.09052
Scale		0.1023	0.04496

Type III Tests of Fixed Effects				
Effect	Num DF	Den DF	F Value	Pr > F
solvent	4	16	49.25	<.0001

-2 log L(counts   r. effects)	
Pearson Chi-Square	202.62
Pearson Chi-Square / DF	23.24
	0.93

# Assessment 1

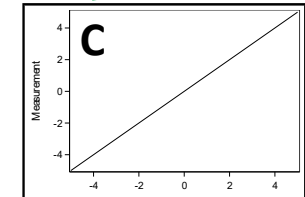
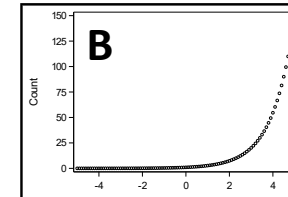
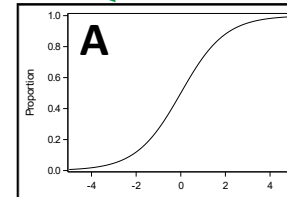


1. You want to run PROC GLIMMIX to model a medical outcome (Med) as a function of a categorical treatment (Treat) with the hospital (Hosp) as a random effect. How would you set up the following SAS code?

```
PROC GLIMMIX data=dataset;
CLASS Treat Hosp;
MODEL Med = Treat;
RANDOM intercept /subject=Hosp;
```

2. Match the following distributions to their appropriate link function (A, B, or C).

- 1) Poisson    2) Negative Binomial    3) Binary    4) Normal



3. Which of the following are likely random effects?

Treatment, **School**, Ethnicity, Temperature, **Block**, Color, Chemical concentration, **Site**

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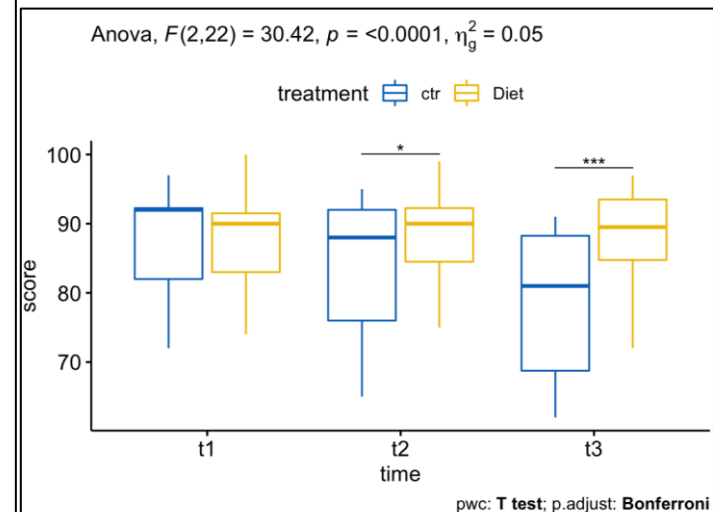
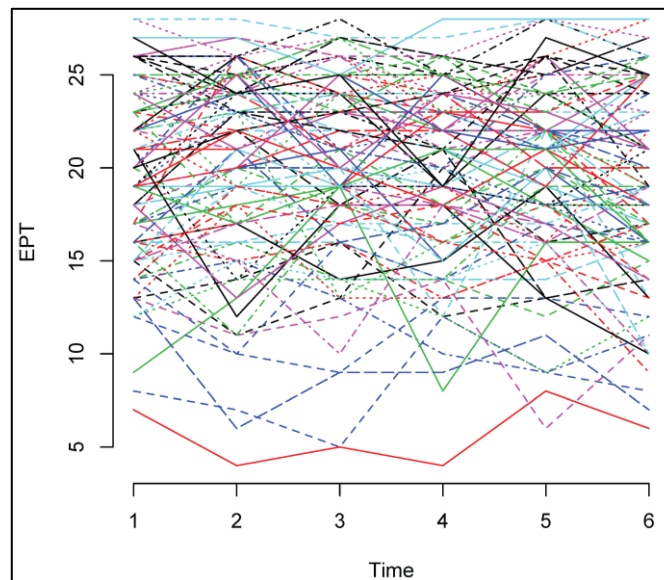
-2 log L(counts   r. effects)	202.62
Pearson Chi-Square	23.24
Pearson Chi-Square / DF	0.93

**Yes, solvent is significant ( $p < 0.05$ ), and colony is non-zero, so it had some effect on the results. The Pearson Chi-Square/DF is around 1.0, so the model is not over dispersed.**

# Longitudinal Analysis

## Descriptions

- Longitudinal data can be viewed as a special case of the multilevel data
- Time is nested within individual participants/observations
- Response variable and predictor variable(s) measured several times
- Point is to characterize change
- Parameters needed to link predictors to response and account for correlational structure of repeated measurements
- Simplest Case: Repeated Measures ANOVA
- Other: Linear mixed effects models, Generalized estimating equations



# Longitudinal Analysis

## Formats

### Repeated Measures ANOVA:

```
aov(Y~TREATMENT*TIME +  
     Error(RANDOM),data=DATASET)
```

```
NESTEDDATASET <- groupedData(Y ~ TREATMENT |  
                              RANDOM, data=DATASET)
```

```
gls(Y ~ TREATMENT*TIME, data=NESTEDDATASET,  
     ❖ corr=corCompSymm(, form= ~ 1 | RANDOM))  
     ❖ corr=corSymm(, form= ~ 1 | RANDOM),  
       weights = varIdent(form = ~ 1 | TIME))  
     ❖ corr=corAR1(, form= ~ 1 | RANDOM))  
     ❖ corr=corAR1(, form= ~ 1 | RANDOM),  
       weights=varIdent(form = ~ 1 | TIME))
```

### Linear Mixed Effects:

*#Random intercept*

```
lmer(Y ~ TREAT + TIME + CAT + (1 | RANDOM), data = DATASET)
```

*#Random intercept and slope*

```
lmer(Y ~ TREAT + TIME + CAT + (TIME | RANDOM), data = DATASET)
```

### Generalized Estimating Equations:

```
glm(Y~ TREATMENT, data=DATASET, family="DISTRUBITION")
```

```
gee(Y~ TREATMENT, data=DATASET, family="DISTRIBUTION", id=RANDOM,  
     ❖ corstr = "independence", scale.fix = TRUE, scale.value = 1)  
     ❖ corstr = "exchangeable", scale.fix = TRUE, scale.value = 1)  
     ❖ corstr = "exchangeable", scale.fix = FALSE, scale.value = 1)
```

# Longitudinal Analysis

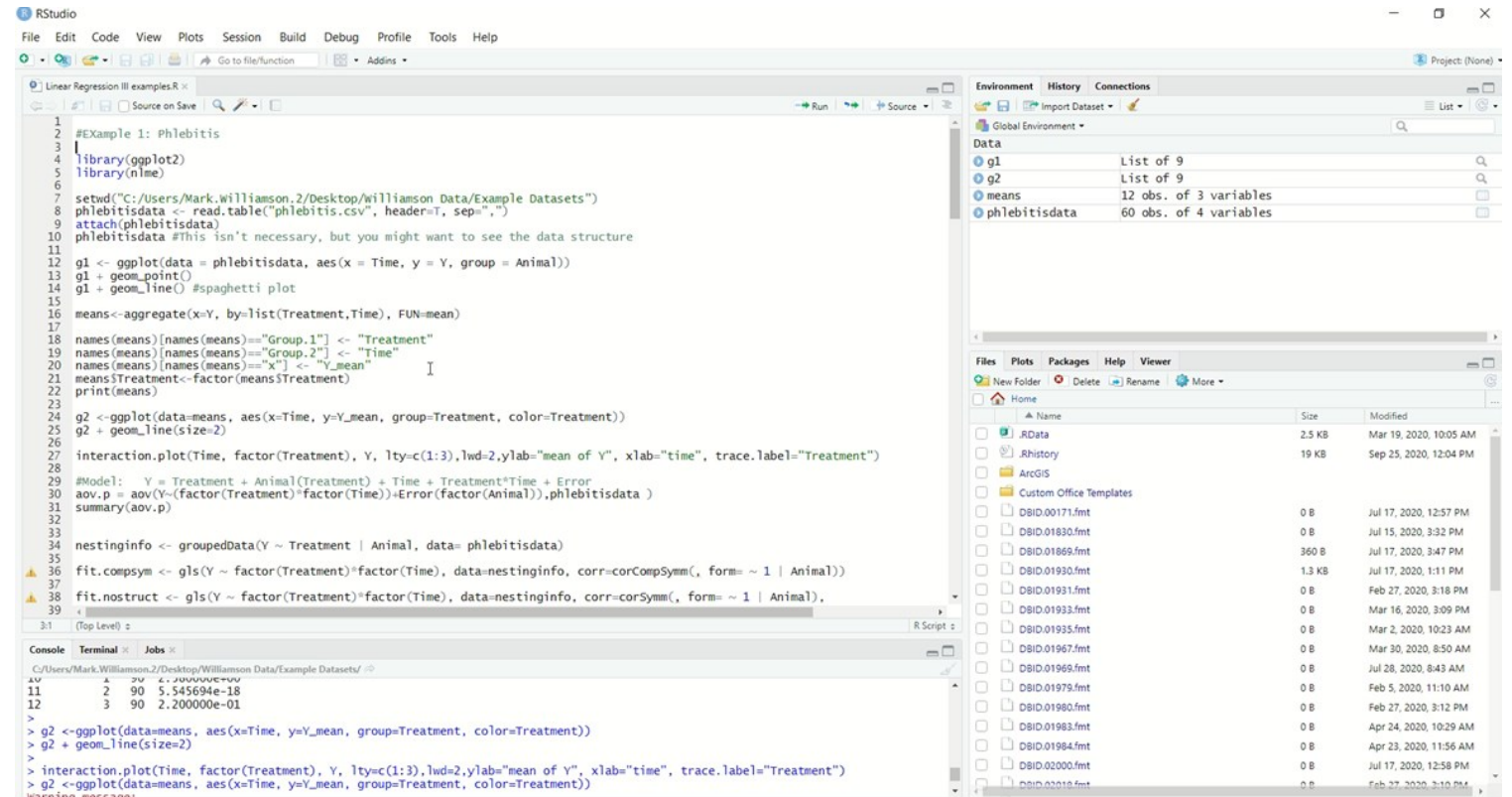
## Examples

Phlebitis (RM-ANOVA)<sup>1</sup>

Beat the Blues (LME)<sup>2</sup>

Respiratory (GEE)<sup>2</sup>

Epilepsy (GEE)<sup>2</sup>



```
1 #Example 1: Phlebitis
2 |
3 |
4 | library(ggplot2)
5 | library(nlme)
6 |
7 | setwd("C:/Users/Mark.Williamson.2/Desktop/williamson Data/Example Datasets")
8 | phlebitisdata <- read.table("phlebitis.csv", header=T, sep=",")
9 | attach(phlebitisdata)
10 | phlebitisdata #This isn't necessary, but you might want to see the data structure
11 |
12 | g1 <- ggplot(data = phlebitisdata, aes(x = Time, y = Y, group = Animal))
13 | g1 + geom_point()
14 | g1 + geom_line() #spaghetti plot
15 |
16 | means <- aggregate(x=Y, by=list(Treatment,Time), FUN=mean)
17 |
18 | names(means)[names(means)=="Group.1"] <- "Treatment"
19 | names(means)[names(means)=="Group.2"] <- "Time"
20 | names(means)[names(means)=="x"] <- "Y_mean"
21 | means$Treatment <- factor(means$Treatment)
22 | print(means)
23 |
24 | g2 <- ggplot(data=means, aes(x=Time, y=Y_mean, group=Treatment, color=Treatment))
25 | g2 + geom_line(size=2)
26 |
27 | interaction.plot(Time, factor(Treatment), Y, lty=c(1:3), lwd=2, ylab="mean of Y", xlab="time", trace.label="Treatment")
28 |
29 | #Model: Y = Treatment + Animal(Treatment) + Time + Treatment*Time + Error
30 | aov.p = aov(Y~(factor(Treatment)*factor(Time))+Error(factor(Animal)), phlebitisdata)
31 | summary(aov.p)
32 |
33 |
34 | nestinginfo <- groupedData(Y ~ Treatment | Animal, data = phlebitisdata)
35 |
36 | fit.compsym <- gls(Y ~ factor(Treatment)*factor(Time), data=nestinginfo, corr=corCompSymm(, form= ~ 1 | Animal))
37 |
38 | fit.nostruct <- gls(Y ~ factor(Treatment)*factor(Time), data=nestinginfo, corr=corSymm(, form= ~ 1 | Animal),
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```

<sup>1</sup><https://online.stat.psu.edu/stat510/lesson/10/10.1>

<sup>2</sup>A Handbook of Statistical Analyses Using R





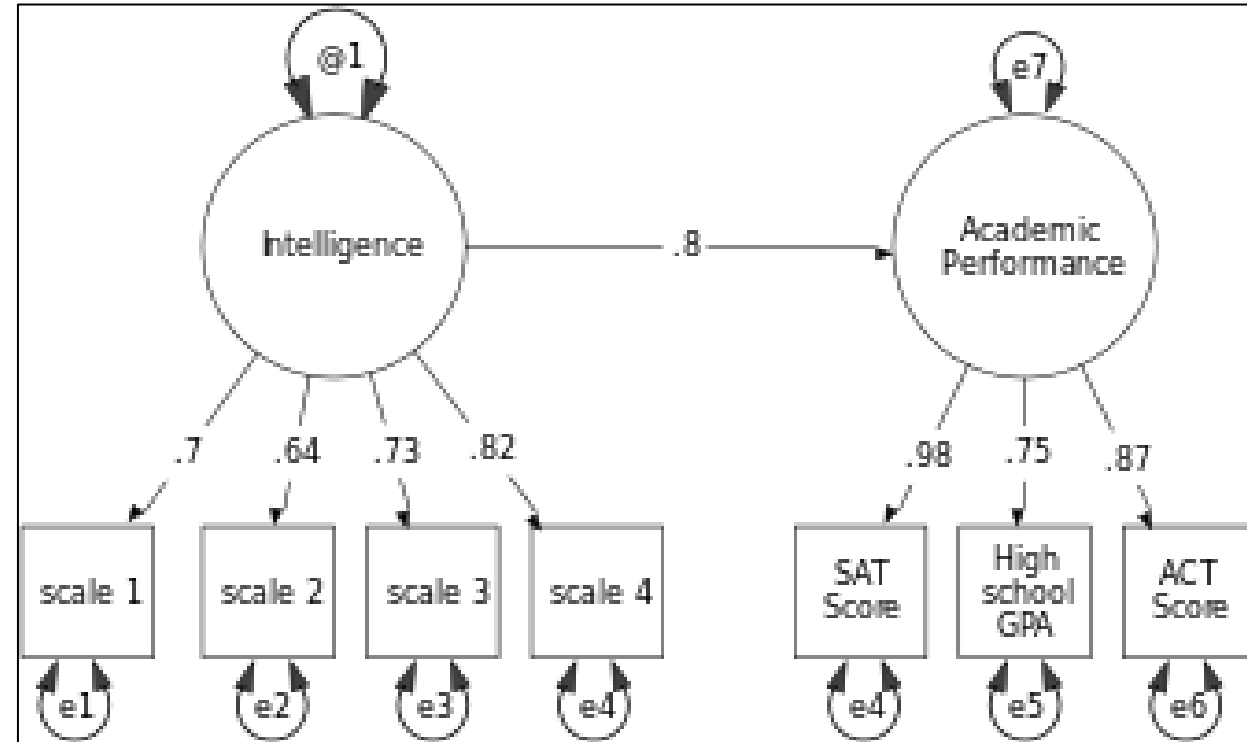


# Structural Equation Modeling

## Descriptions

- Multivariate statistical analysis-> factor analysis combined with multiple regression analysis
- Can be used to impute relationships between unobserved constructs (latent variables) from observable variables
- General approach
  - Model specification
  - Estimation of free parameters
  - Assessment of model and model fit
  - Model modification
  - Sample size and power
  - Interpretation and communication

- **Boxes: observed variables**
- **Circles: unobserved (latent) variables**
- **Arrows: paths**
  - **pointing: first variable affects the second (First -> Second)**
  - **small number is the value of constrained path coefficient**
  - **no number, then coefficient estimated from the data**
- **Curved, double headed paths: covariance (not otherwise assumed, like exogenous variables)**



An example structural equation model. Latent variables are drawn as circles. Manifest or measured variables are shown as squares. Residuals and variances are drawn as double headed arrows into an object. Note latent IQ variable fixed at 1 to provide scale to the model (Wikipedia)

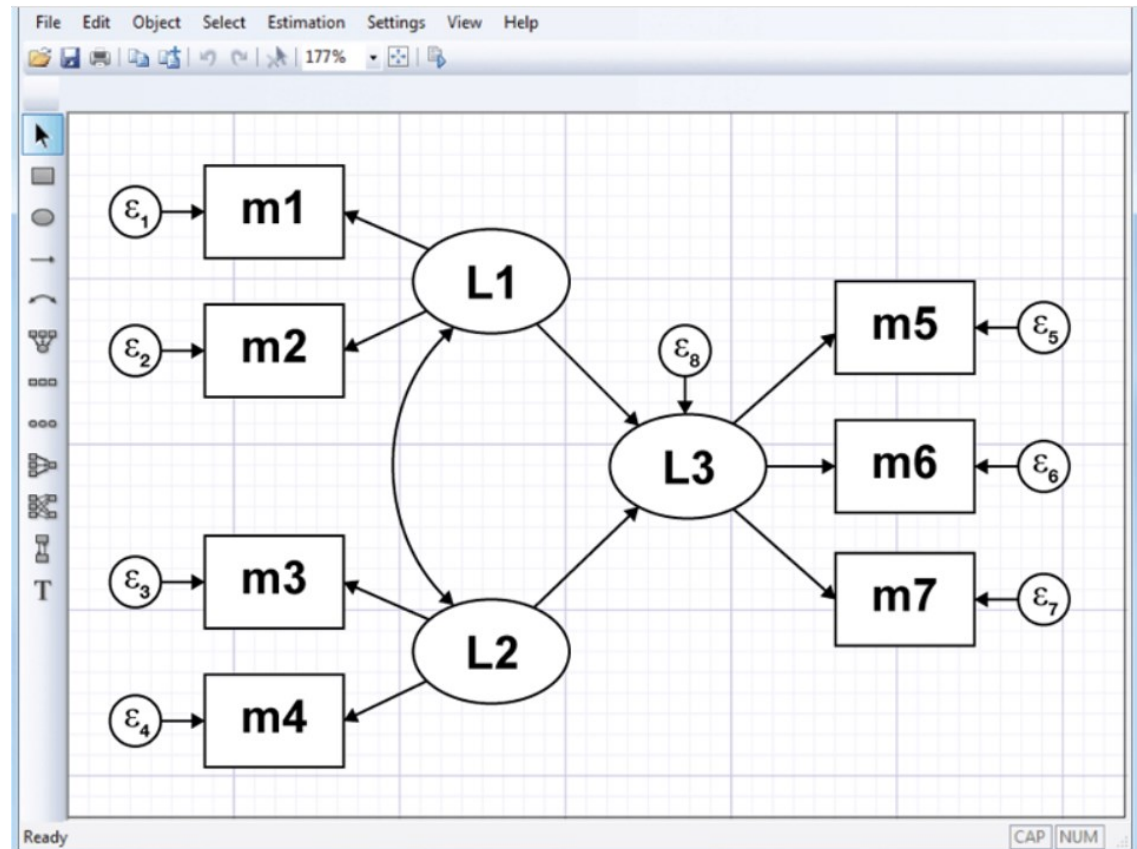
# Structural Equation Modeling

## Formats

### Command Line:

```
. sem (L1 -> m1 m2)  
      (L2 -> m3 m4)  
      (L3 <- L1 L2)  
      (L3 -> m5 m6 m7)  
  
. sem (m1 <- L1) (m2 <- L1) (L2 -> m3) (L2 -> m4)  
(L3 -> m5) (L3 -> m6) (L3 -> m7) (L3 <- L1) (L3 <- L2)  
cov(e.m1*e.m2) cov (e.L1*e.L2)
```

### Graphically:



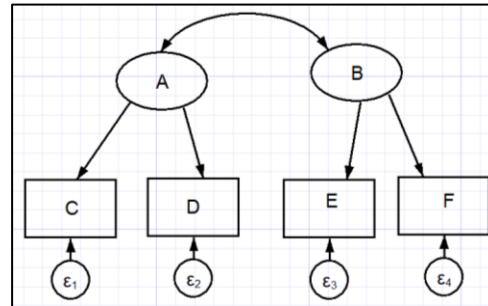




# Assessment 3



1. In the mock SEM diagram below, what type of variable does B represent? What about E?



2. Which of the following Stata commands would include the covariance between VarA and VarB?

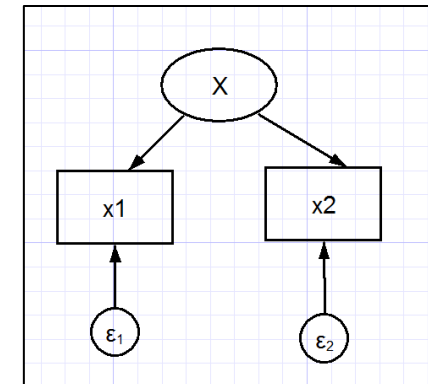
- a) `cov(e.VarA) cov(e.VarB)`
- b) `cov(e.VarA*e.VarB)`
- c) `cov(e.VarA, e.VarB)`
- c) `cov(e.VarA e.VarB)`

3. Looking at the fit of a SEM model returned the values below. Is the model a good fit? Why or why not?

LR test model vs. saturated:  $\chi^2(4) = 4.78, \text{Prob} > \chi^2 = 0.3111$

4. What is the proper line path for the SEM diagram to the right?

- a) `(x1 x2 <- X)`
- b) `(x1 x2 -> X)`
- c) `(X <- x1 x2)`
- d) `(X <- x1 <- x2)`

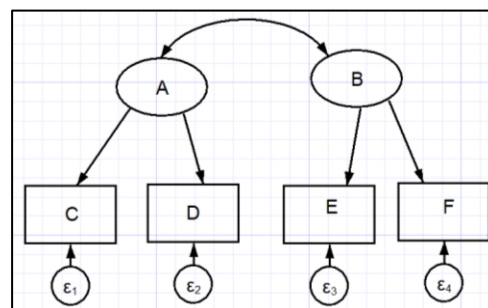


# Assessment 3



1. In the mock SEM diagram below, what type of variable does B represent? What about E?

**B represents a latent, or unobserved variable (circle). E represents an observed variable (square).**



2. Which of the following Stata commands would include the covariance between VarA and VarB?

- a) `cov(e.VarA) cov(e.VarB)`
- b) `cov(e.VarA*e.VarB)`
- c) `cov(e.VarA, e.VarB)`
- c) `cov(e.VarA e.VarB)`

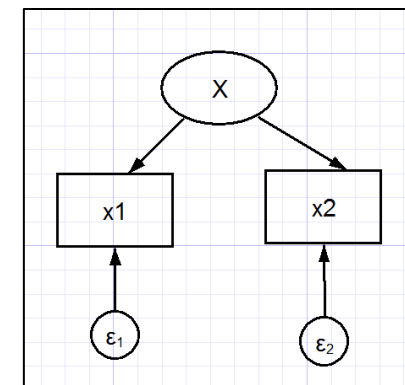
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LR test model vs. saturated:  $\chi^2(4) = 4.78, \text{Prob} > \chi^2 = 0.3111$

**The test about if the model against a saturated model. Because the probability is not significant ( $\geq 0.05$ ), the model is a good fit because there is no indication that adding more paths would improve the fit.**

4. What is the proper line path for the SEM diagram to the right?

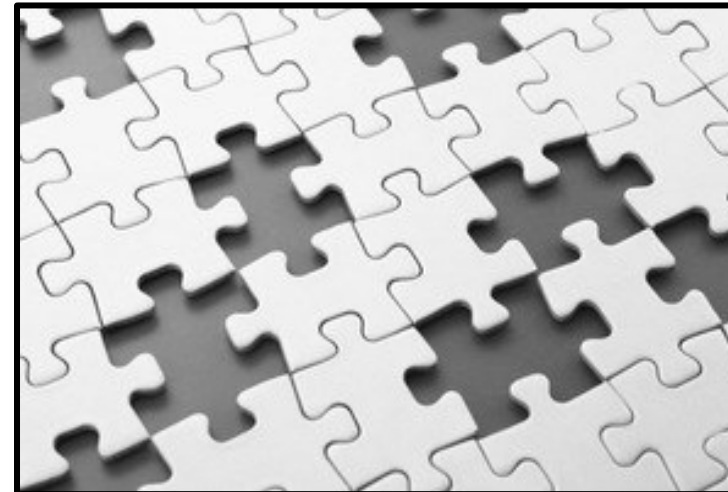
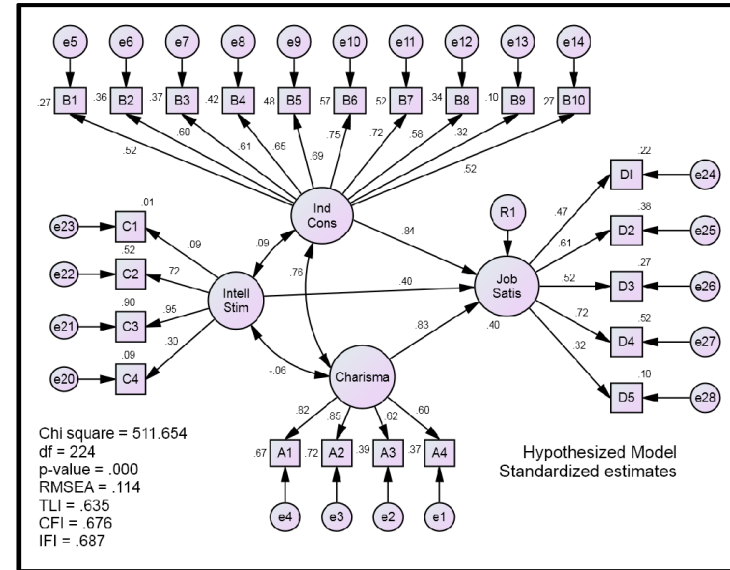
- a) `(x1 x2 <- X)`
- b) `(x1 x2 -> X)`
- c) `(X <- x1 x2)`
- d) `(X <- x1 <- x2)`



# Caveats and Concerns



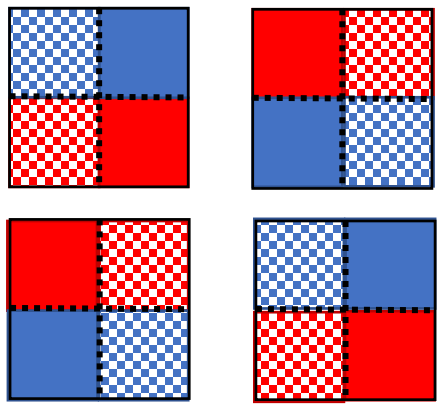
- More complex analyses come with more work and understanding
  - Multiple models, assumptions, and tests
- Data issues:
  - Restructuring
  - Reformatting
  - Missing data
- May need to try different software to get the job done



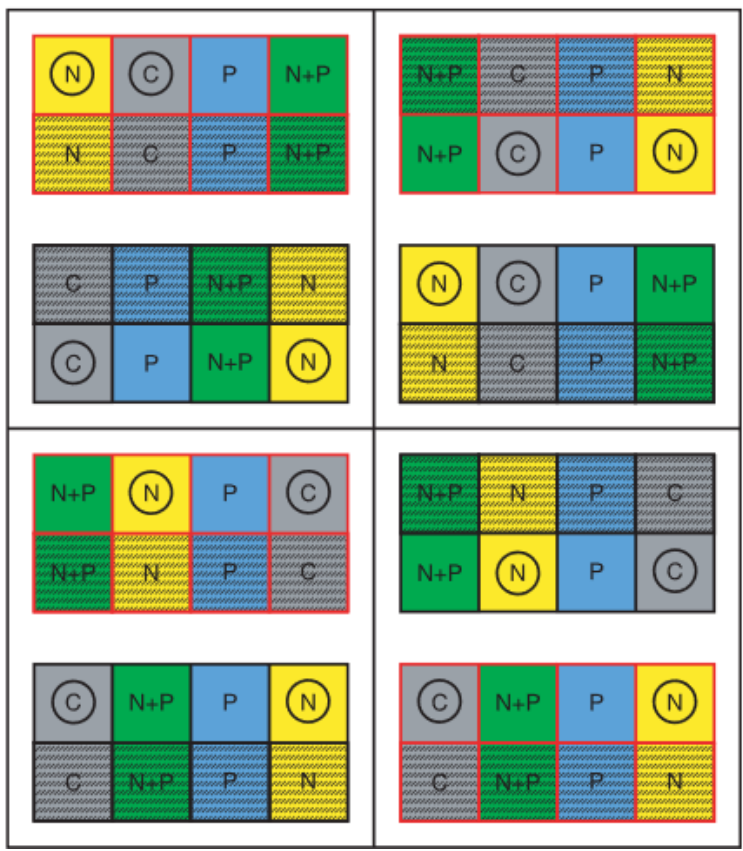
# Real World Examples

JONES, K. L., TODD, T. C., WALL-BEAM, J. L., COOLON, J. D., BLAIR, J. M., & HERMAN, M. A. (2006). Molecular approach for assessing responses of microbial-feeding nematodes to burning and chronic nitrogen enrichment in a native grassland. *15*(9), 2601-2609. doi:10.1111/j.1365-294X.2006.02971.x

Strip-Split



random block  
 block\*color  
 block\*shading;



**Fig.1** The field experimental design included eight whole plots grouped into four blocks, with one plot per block that was burned annually (red outline) or left unburned (black outline). A split-strip plot design was obtained by mowing (hatched plots) or not mowing (open plots) one-half of each whole plot (i.e. the whole plots were split by mowing treatment) and using nutrient enrichment [nitrogen (N), phosphorous (P), both (N + P), or neither (C)] as a strip treatment applied perpendicular across the mowing treatments of each block. For this study, we sampled the 16 subplots (circled) that were not mowed, and had either nitrogen enrichment alone or had no nutrient addition. Thus, the four treatment combinations sampled were burned with and without nitrogen addition, and unburned with and without nitrogen addition.

# Real World Examples

Doll, R., & Hill, A. B. (2004). The mortality of doctors in relation to their smoking habits: a preliminary report. 1954. *BMJ (Clinical research ed.)*, 328(7455), 1529-1533.  
 doi:10.1136/bmj.328.7455.1529

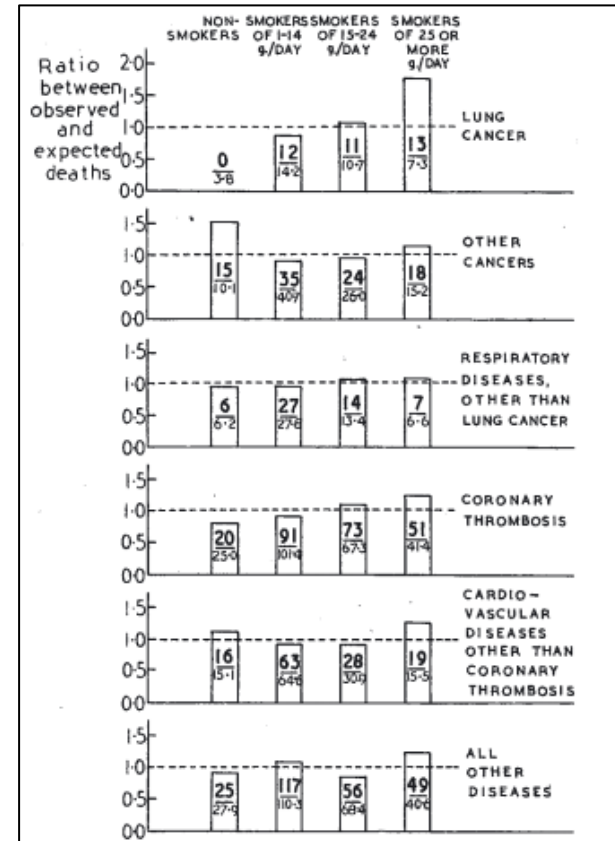
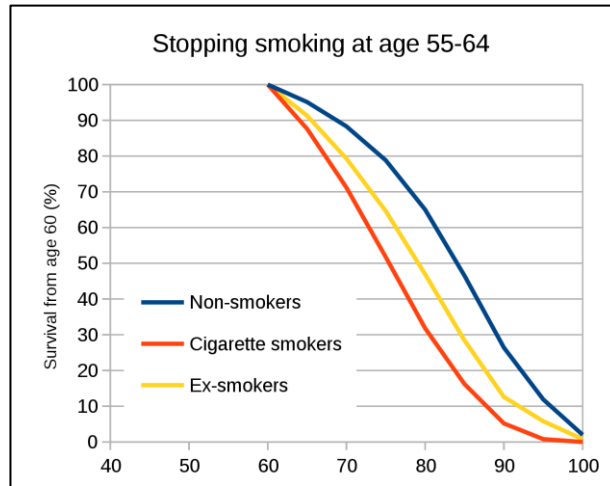
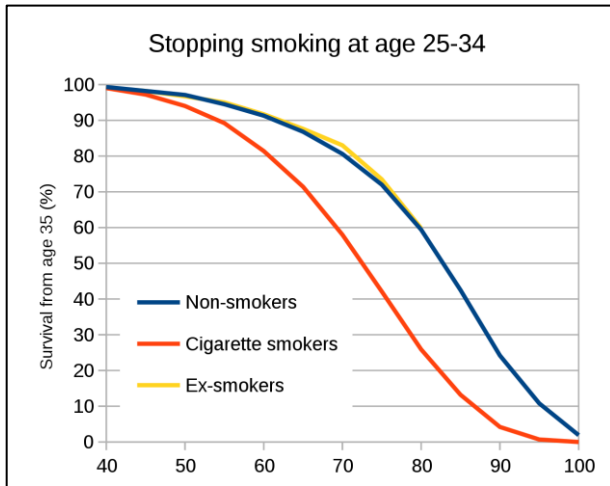


Chart showing variation in mortality with amount smoked. The ordinate shows the ratio between the number of deaths observed and the number expected (as entered in each column).



# Real World Examples

Schwartz, G. G., & Klug, M. G. (2019). Thyroid Cancer Incidence Rates in North Dakota are Associated with Land and Water Use. *International Journal of Environmental Research and Public Health*, 16(20). doi:10.3390/ijerph16203805

Schwartz, G. G., Klug, M. G., & Rundquist, B. C. (2019). An exploration of colorectal cancer incidence rates in North Dakota, USA, via structural equation modeling. *International Journal of Colorectal Disease*, 34(9), 1571-1576. doi:10.1007/s00384-019-03352-9

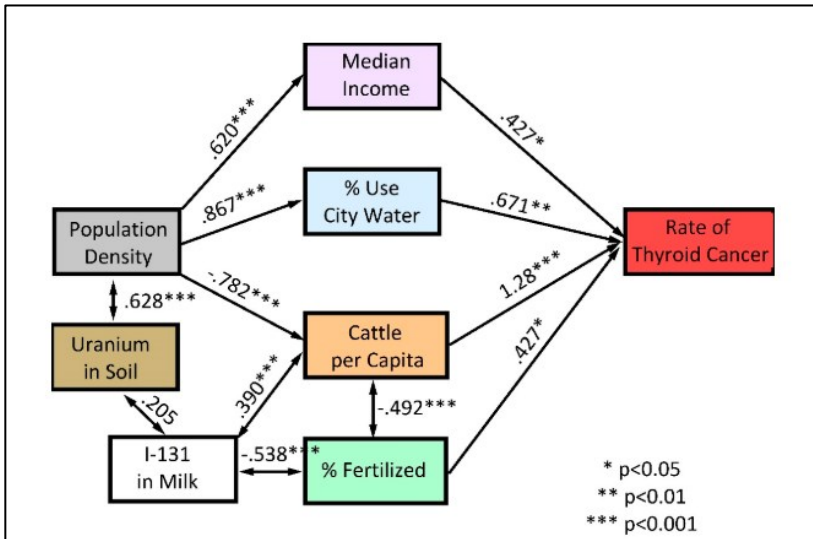


Figure 2. Structural Equation Model for county-specific thyroid cancer incidence rates in North Dakota. Uni-directional arrows indicate potential causal pathways. Bi-directional arrows indicate a co-varying relationship that is unlikely to be causal.

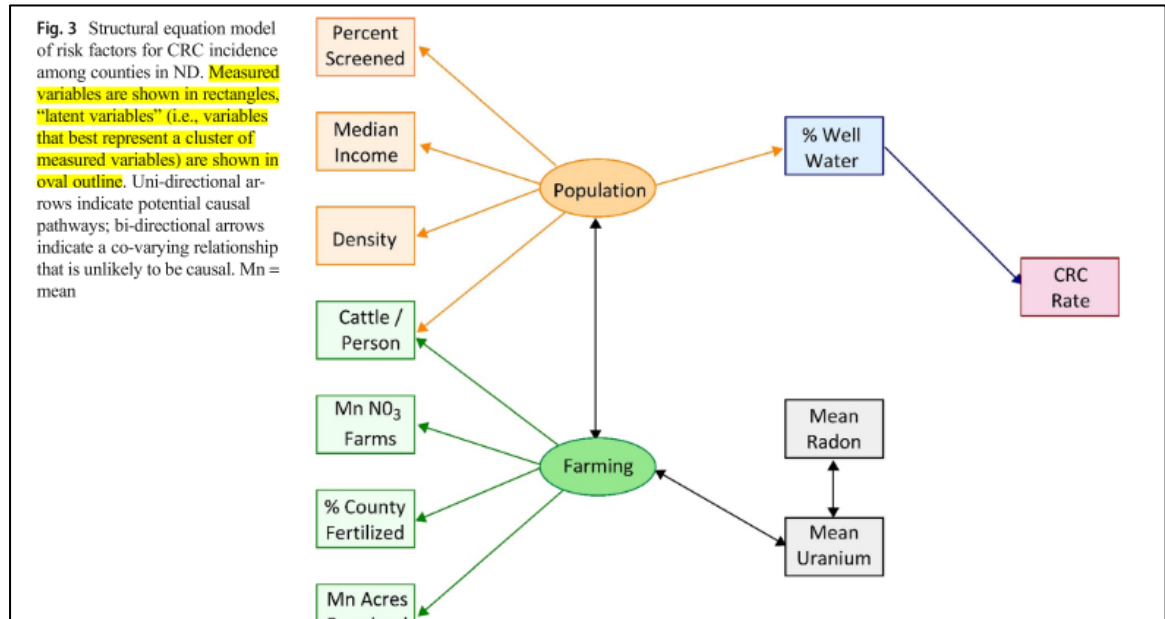
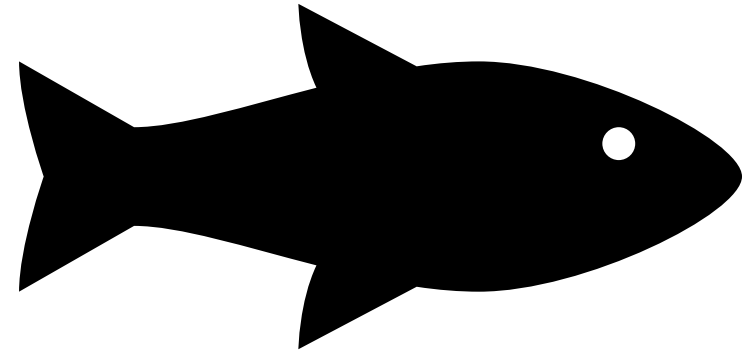


Fig. 3 Structural equation model of risk factors for CRC incidence among counties in ND. Measured variables are shown in rectangles. "latent variables" (i.e., variables that best represent a cluster of measured variables) are shown in oval outline. Uni-directional arrows indicate potential causal pathways; bi-directional arrows indicate a co-varying relationship that is unlikely to be causal. Mn = mean

# Summary and Conclusion

- There are lots of advanced regression approaches
- Approach depends on data and questions asked
- Requires more work, understanding, and patience the more complex it is
- R, SAS, and STATA all have procedures for advanced approaches



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