Meta-Analysis: Part 1
Lecture

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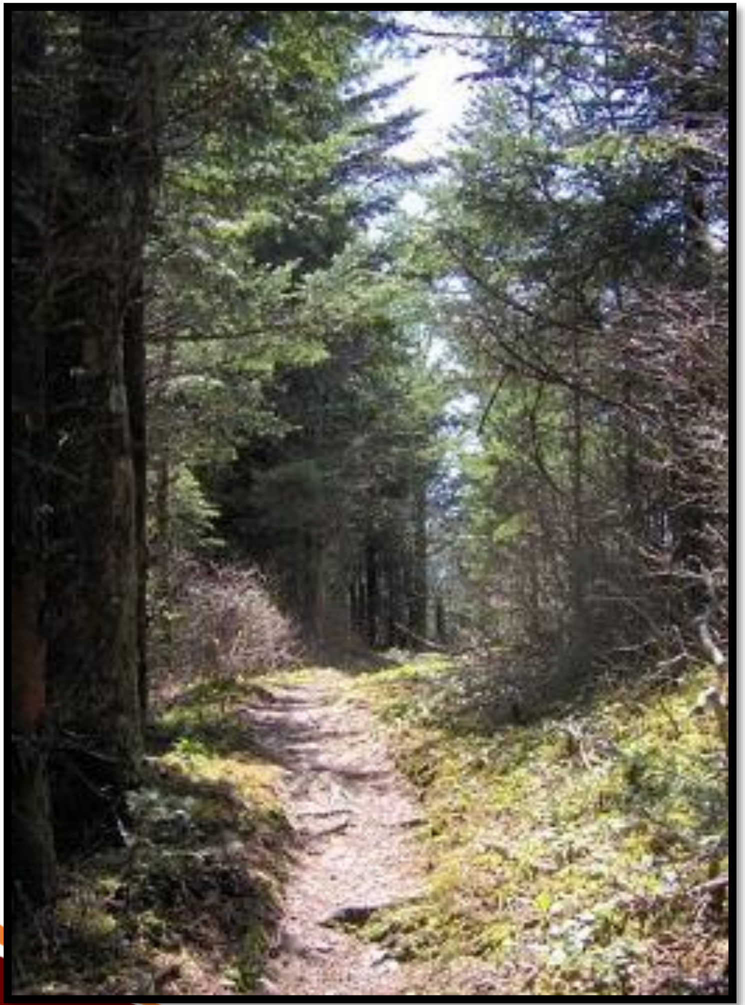
A Roadmap…



- Why conduct meta-analyses?
- A brief history of meta-analysis
- Prepping data for meta-analysis
- The modern meta-analysis
- Follow up analyses

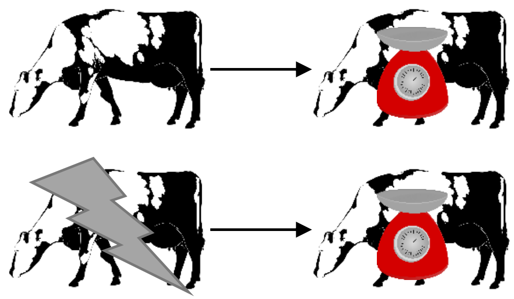
Why Summarize Literature?

The human brain and the scientific method are limited…

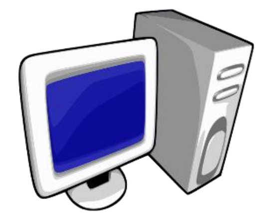
The Hypothesis

The Conclusion

The Experiment



The Analysis



The Common Problem:

Study	1	2	3	4	5
Conclusion					

Quantitative literature synthesis helps simplify reality.

Challenges with Biological Data

Treatment	Milk	SE
1	25.4	1.5
2	30.6	2.8


An Evaluation of Postabsorptive Protein and Amino Acid Metabolism in the Lactating Dairy Cow

M. D. HANIGAN, J. P. CANT, D. C. WEAKLEY, and J. L. BECKETT

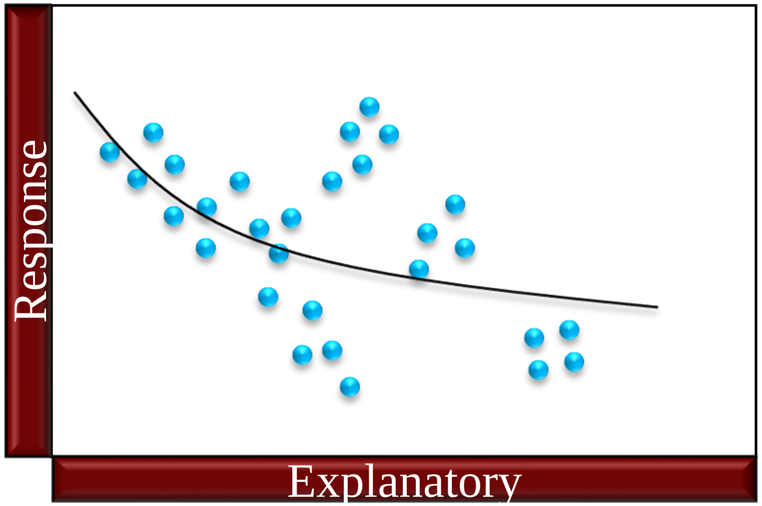
ABSTRACT

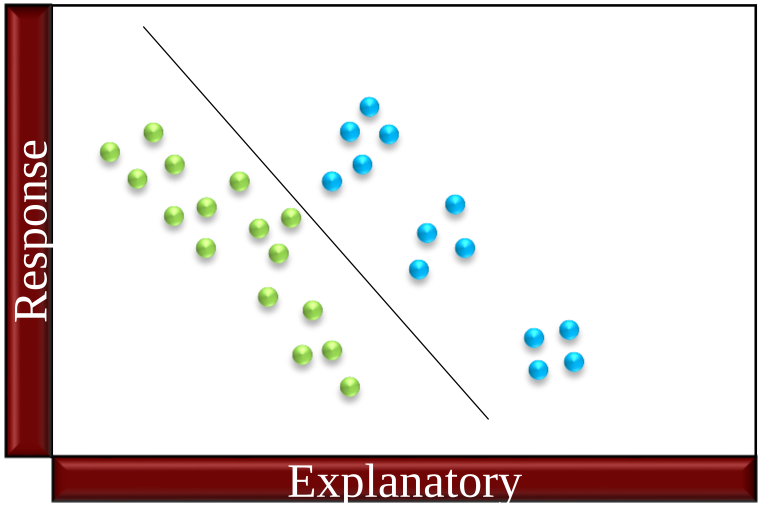
INTRODUCTION

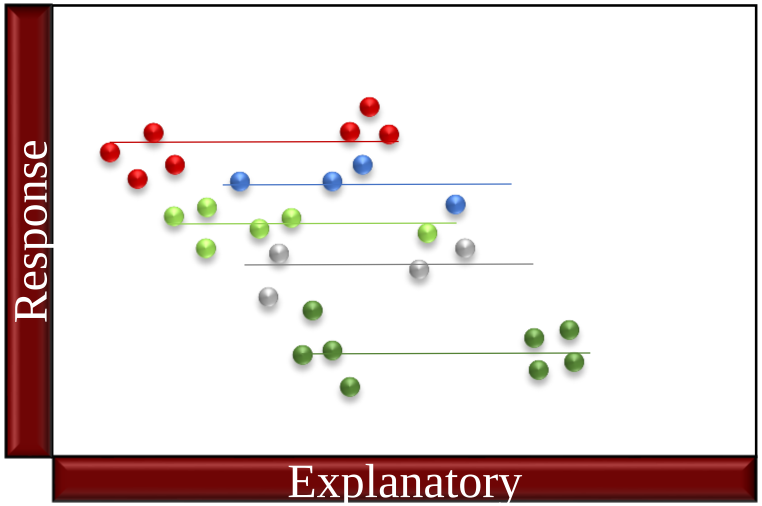
Partitioning Variability

1. Variability within an animal
2. Variability between animals
3. Variability induced by treatments
4. Variability between measurement methods, locations, researchers, etc.
5. Variability associated with everything else you didn't measure

Partitioning Variability







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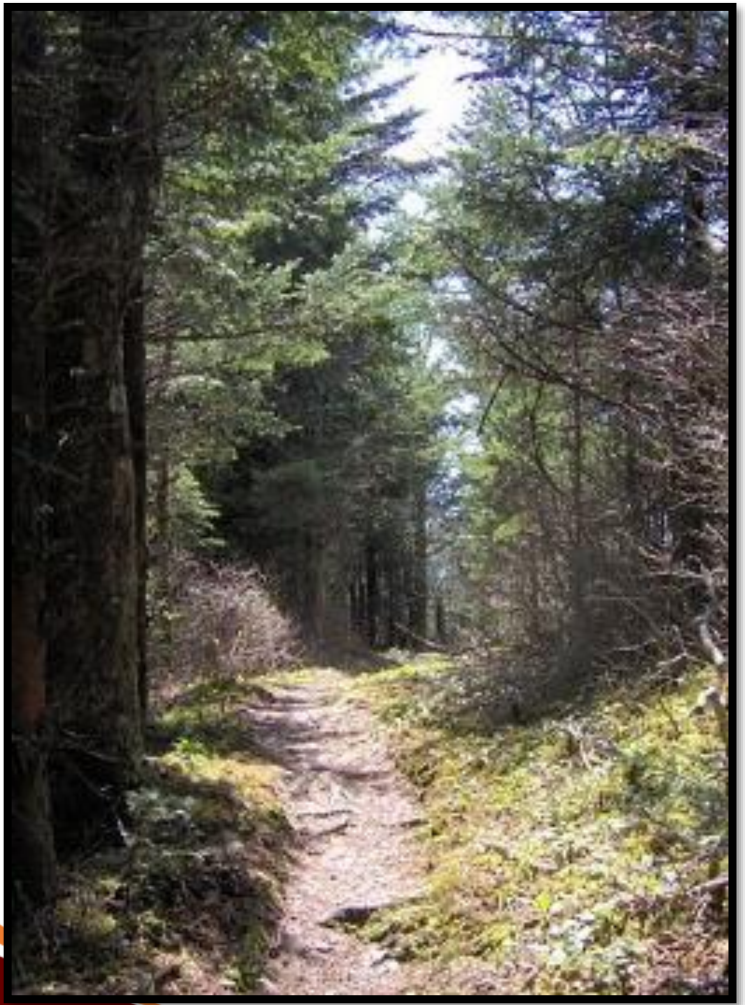
How did meta-analysis come about?



Why conduct meta-analyses?

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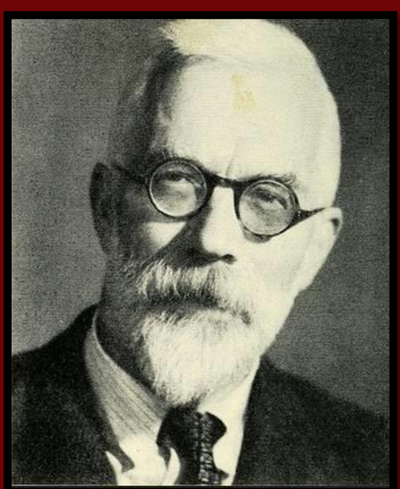
Follow up analyses

The Driving Force Behind Meta-Analysis

The Common Problem:

Study	1	2	3	4	5
Conclusion					



R.A. Fisher (1944) – "When a number of quite independent test of significance have been made, it sometimes happens that although few of none can be claimed individually as significant, yet the aggregate gives an impression that the probabilities are on the whole lower than would often have been obtained by chance"

A Brief History of Advancement

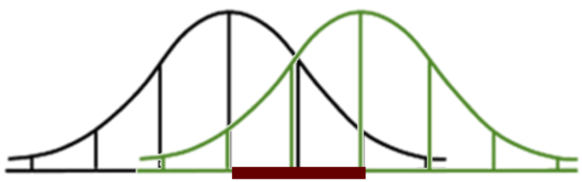
1904, Karl Pearson publishes first summary of studies

1940, Pratt et al. publish the first summary of identical experiments on the same topic

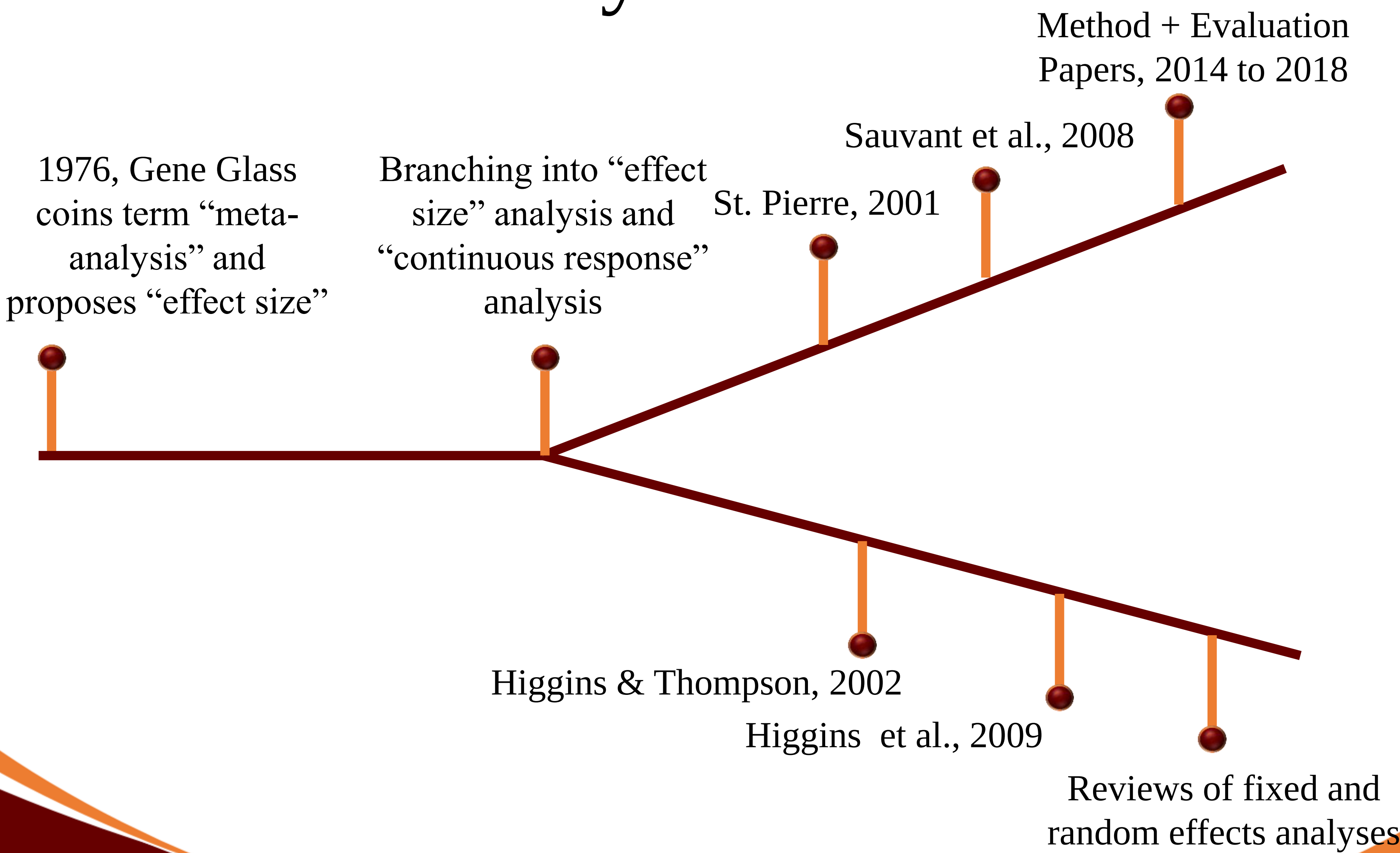
1944, Fisher notices a pattern

1955, First meta-analysis of the efficacy of a medical treatment

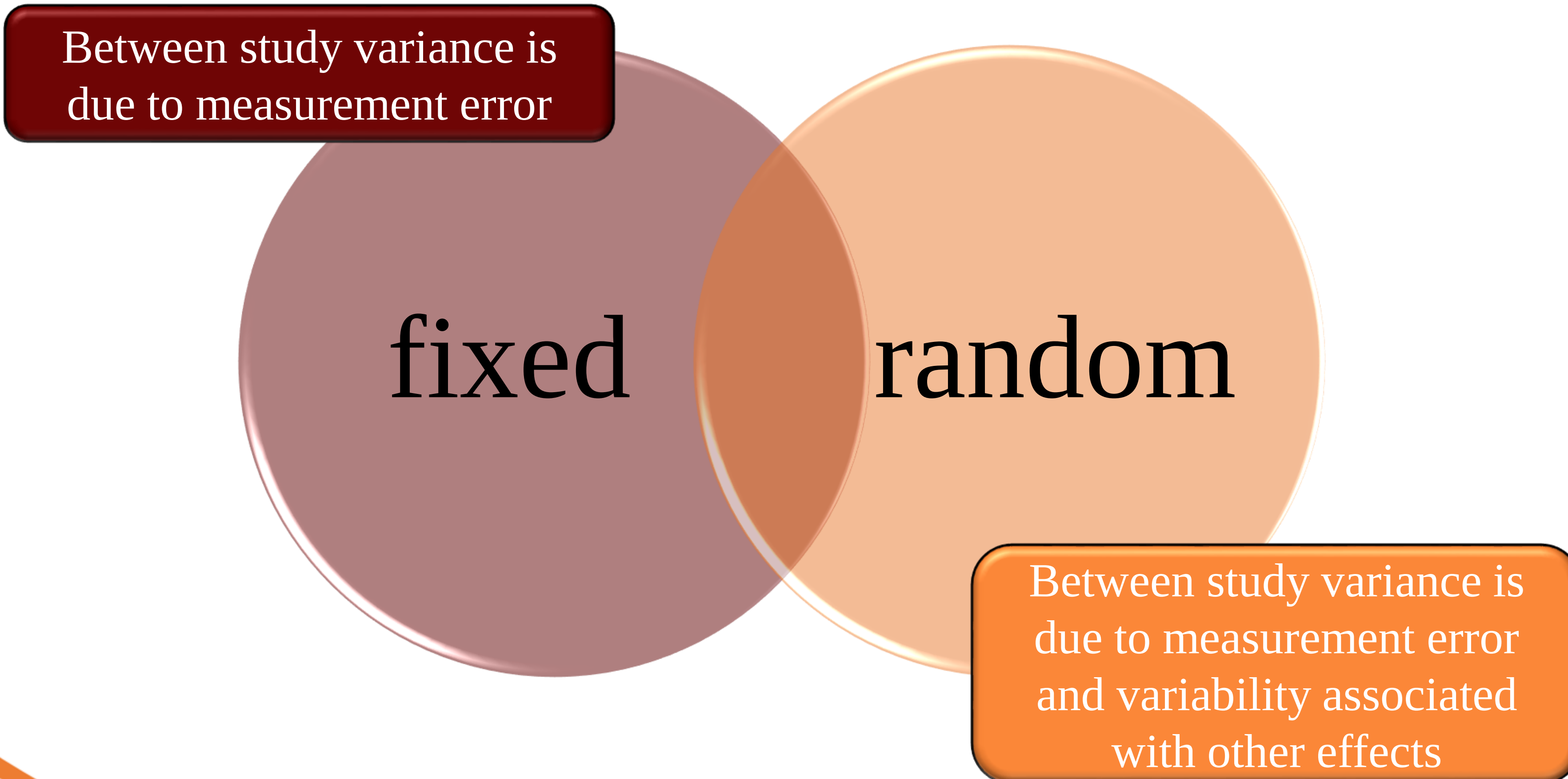
1976, Gene Glass coins term "meta-analysis" and proposes "effect size"



A Brief History of Advancement



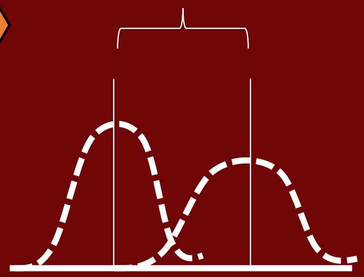
Effect Size Based Analysis



Effect Size Based Analysis

Treatment	Milk	SE
Control	25.0	1.5
Treatment	30.5	2.8

Effect Size



A Common Approach:

1. Identify treatment and control for each study
2. Calculate effect size or standardized difference
3. Conduct fixed-effect analysis, test heterogeneity
4. Move on to random-effect analysis if significant heterogeneity exists

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Use of the Metafor Package in R

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The metafor Package
A Meta-Analysis Package for R

Trace: · **Homepage**

metafor

Navigation

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The metafor Package: A Meta-Analysis Package for R

The metafor package is a free and open-source add-on for conducting meta-analyses with the statistical software environment R. The package consists of a collection of functions that allow the user to calculate various effect size or outcome measures, fit fixed-, random-, and mixed-effects models to such data, carry out moderator and meta-regression analyses, and create various types of meta-analytical plots.

On this website, you can find:

- some news concerning the package and/or its development,
- a more detailed description of the package features,
- a log of the package updates that have been made over the years,
- a to-do list and a description of planned features to be implemented in the future,

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Data Setup

The contents of the dataset are:

	trial	author	year	tpos	tneg	cpos	cneg	ablat	alloc
1	1	Aronson	1948	4	119	11	128	44	random
2	2	Ferguson & Simes	1949	6	300	29	274	55	random
3	3	Rosenthal et al	1960	3	228	11	209	42	random
4	4	Hart & Sutherland	1977	62	13536	248	12619	52	random
5	5	Frimodt-Moller et al	1973	33	5036	47	5761	13	alternate
6	6	Stein & Aronson	1953	180	1361	372	1079	44	alternate
7	7	Vandiviere et al	1973	8	2537	10	619	19	random
8	8	TPT Madras	1980	505	87886	499	87892	13	random
9	9	Coetzee & Berjak	1968	29	7470	45	7232	27	random
10	10	Rosenthal et al	1961	17	1699	65	1600	42	systematic
11	11	Comstock et al	1974	186	50448	141	27197	18	systematic
12	12	Comstock & Webster	1969	5	2493	3	2338	33	systematic
13	13	Comstock et al	1976	27	16886	29	17825	33	systematic

Calculate Risk Ratio and Run Model

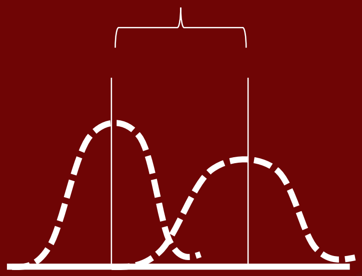
```r
dat <- escalc(measure="RR", ai=tpos, bi=tneg, ci=cpos, di=cneg, data=dat.bcg)
```

```r
res.RE <- rma(yi, vi, data=dat, method="EB")
res.RE
```

```
Random-Effects Model (k = 13; tau^2 estimator: EB)

tau^2 (estimated amount of total heterogeneity): 0.2682 (SE = 0.1801)
tau (square root of estimated tau^2 value):      0.5178
I^2 (total heterogeneity / total variability):   87.49%
H^2 (total variability / sampling variability):  7.99

Test for Heterogeneity:
Q(df = 12) = 85.8625, p-val < .0001

Model Results:

estimate       se     zval     pval    ci.lb    ci.ub
 -0.5429   0.1842  -2.9474   0.0032  -0.9040  -0.1819      **

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Other Features

Effect Size



Moderators:

Capacity to analyze how continuous factors influence effect size

Multi-Level Effects:

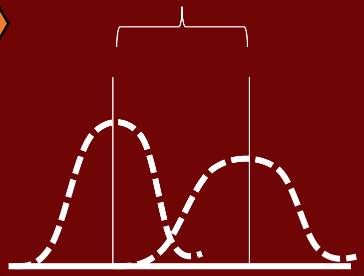
Capacity to analyze how continuous factors influence effect size

One Caution

Inputted SEM is used to compute known error variance

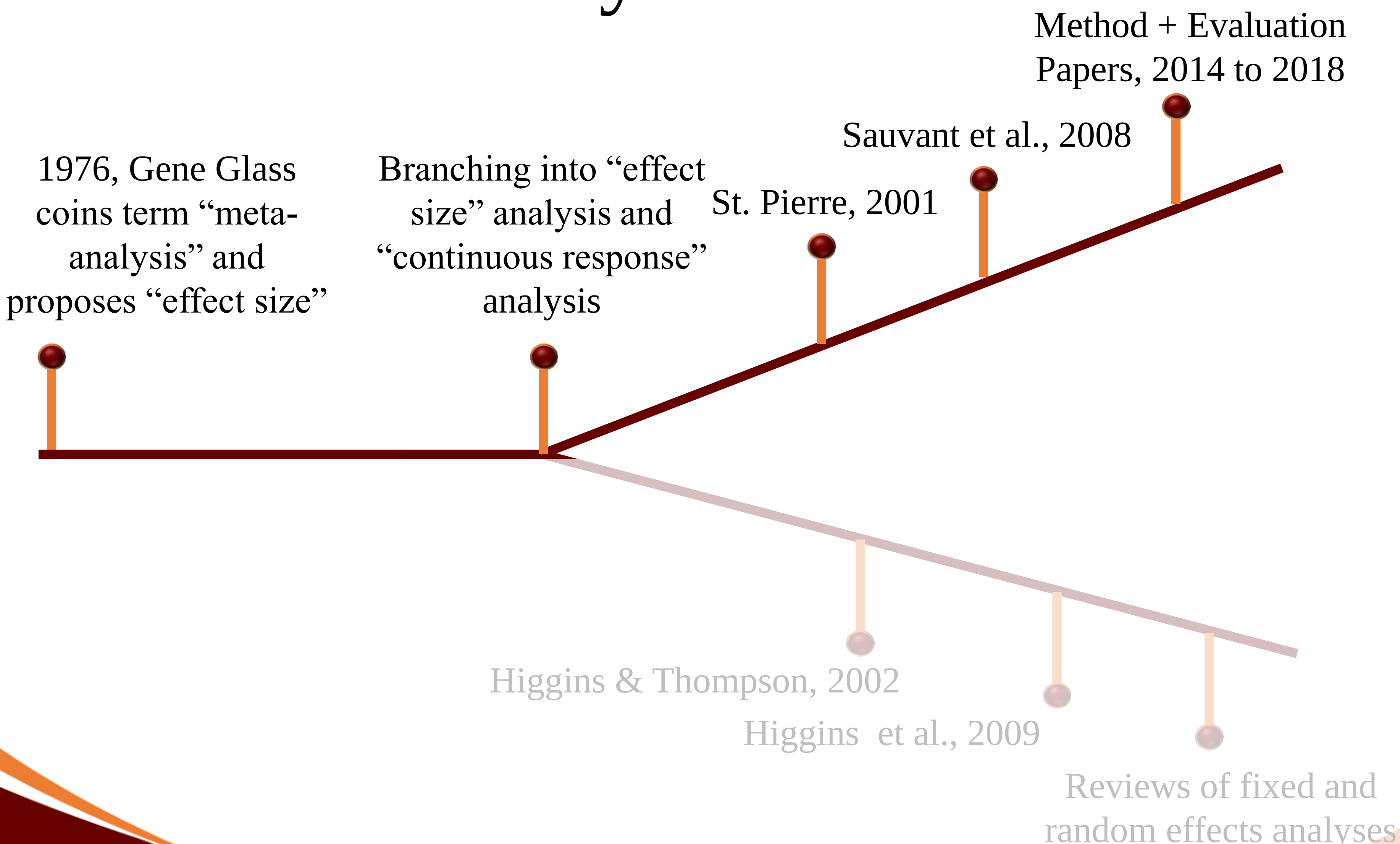
Treatment	Milk	SE
Control	25.0	1.5
Treatment	30.5	2.8

Effect Size



Perhaps not justifiable in most scenarios.
Concern when SEM are adjusted for study/analysis differences.

A Brief History of Advancement



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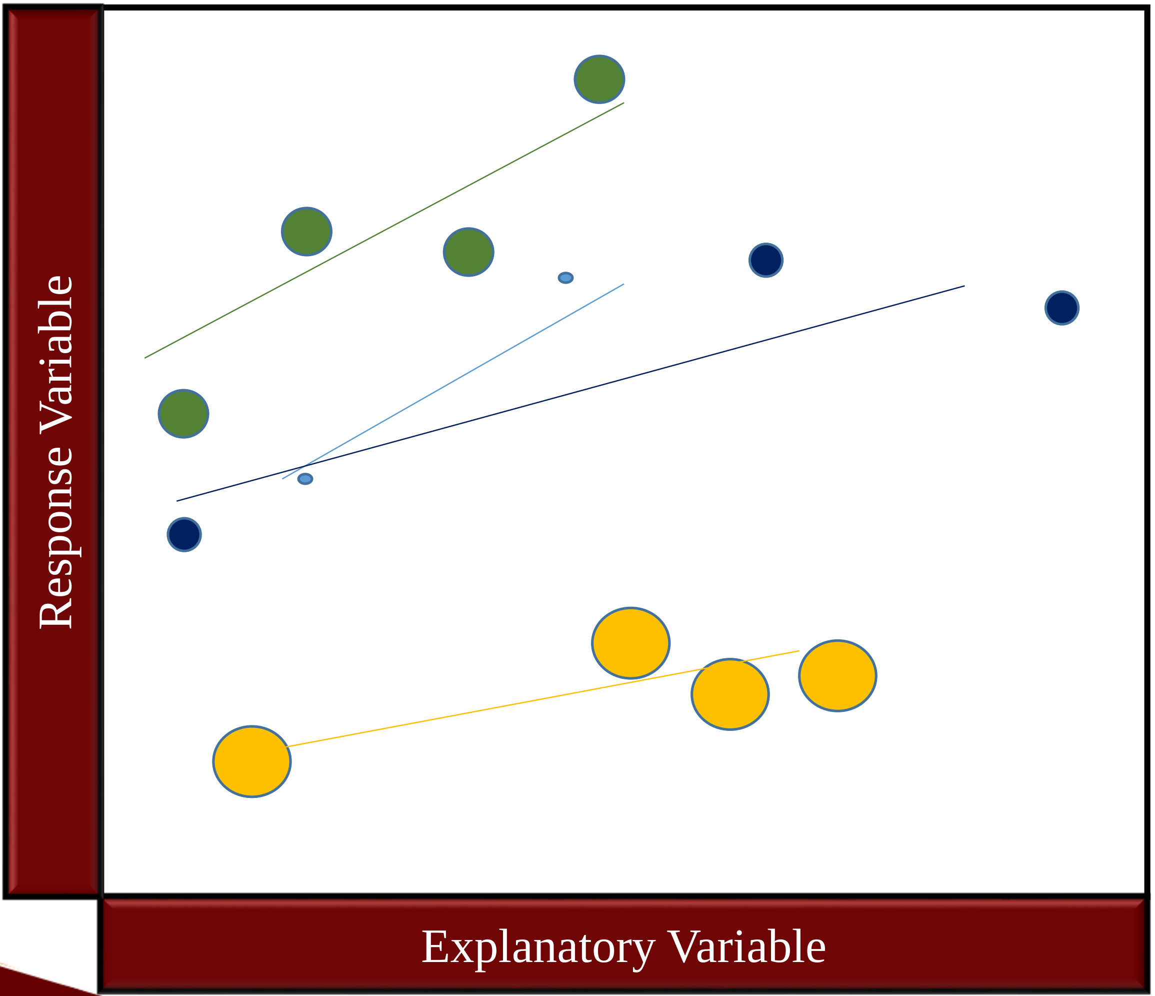
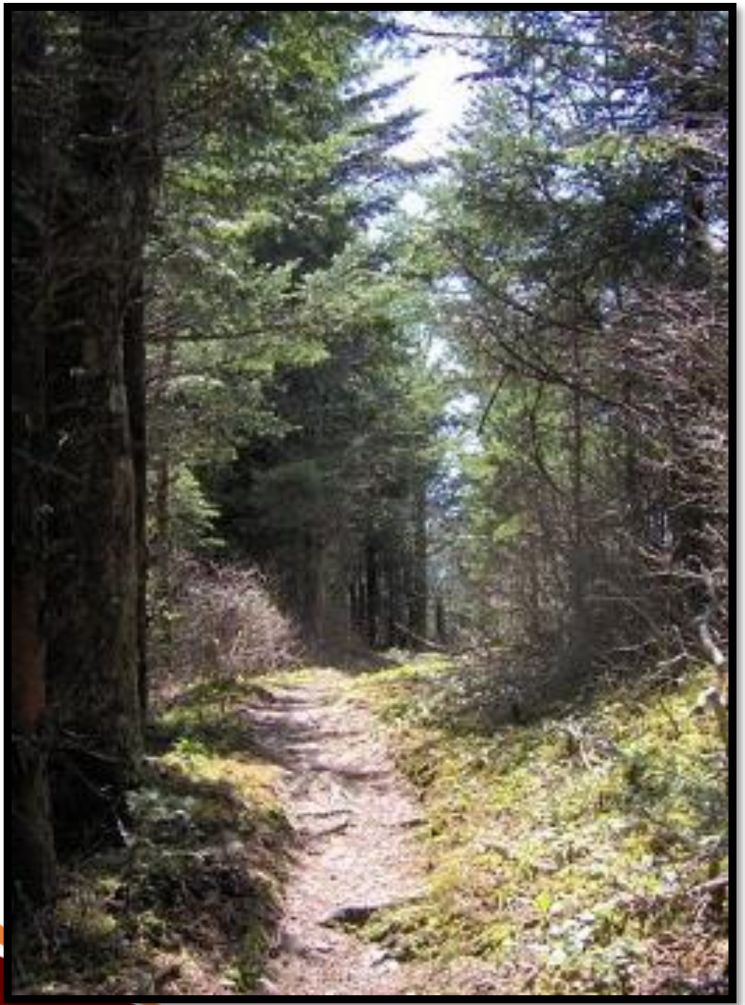
The "Modern" Meta-Regression

Using mixed models, weighted for study precision, and a random effect for study to evaluate responses in a continuous variable



First Steps to Conducting Analysis



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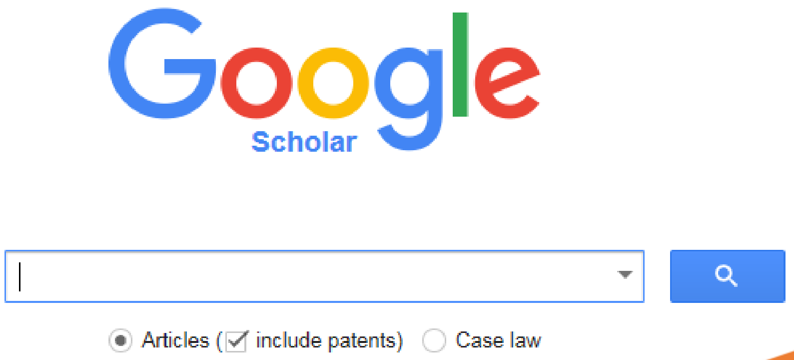
Approach to Data Handling

- **Select search parameters**
- Define all variables of interest
- Formalize inclusion criteria
- Search for papers and record results
- Define exclusion criteria



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- List potential response variables
- All response variables must have SE
- List any explanatory variable
  - Experimental
  - Biological
  - Geographical
  - Etc.

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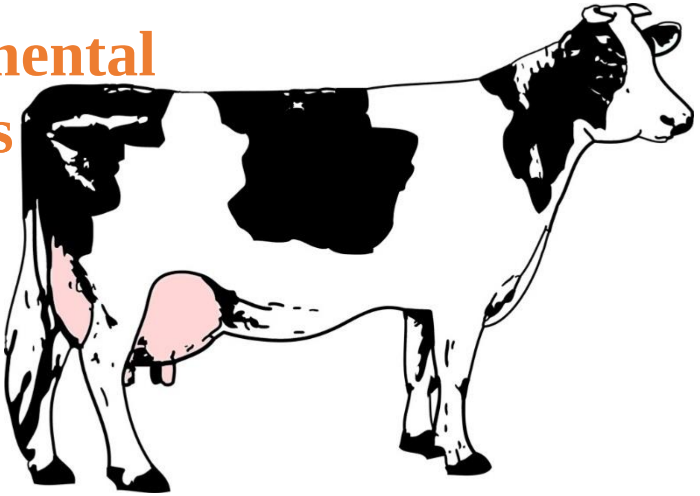
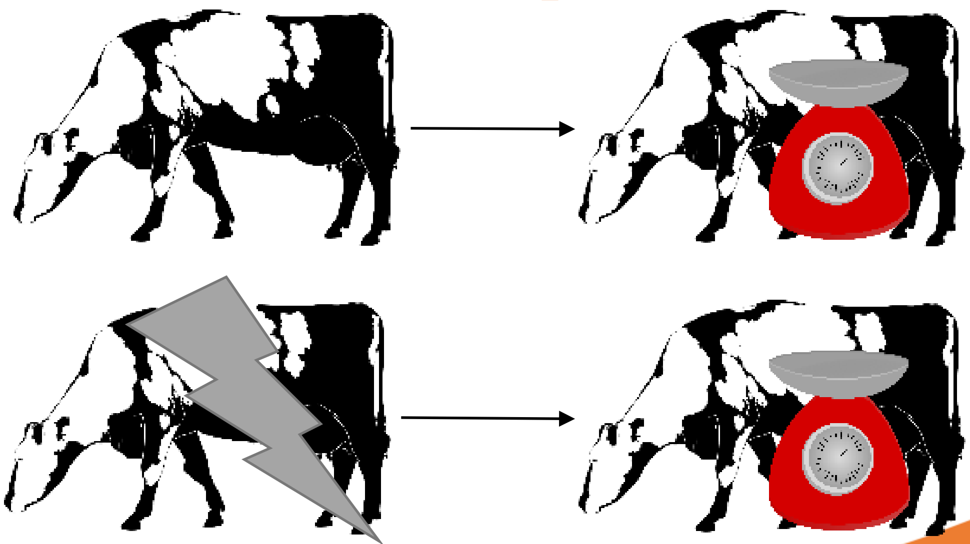
Experimental Subjects



Experimental Designs



Approach to Data Handling

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- Use Excel or googlesheets to house data
- Give each study and each treatment a unique ID #
- Save a copy of each pdf in a folder, labeled with the same ID as is used in the data
- Input the citation information into your reference manager

Approach to Data Handling

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Screen for Outliers

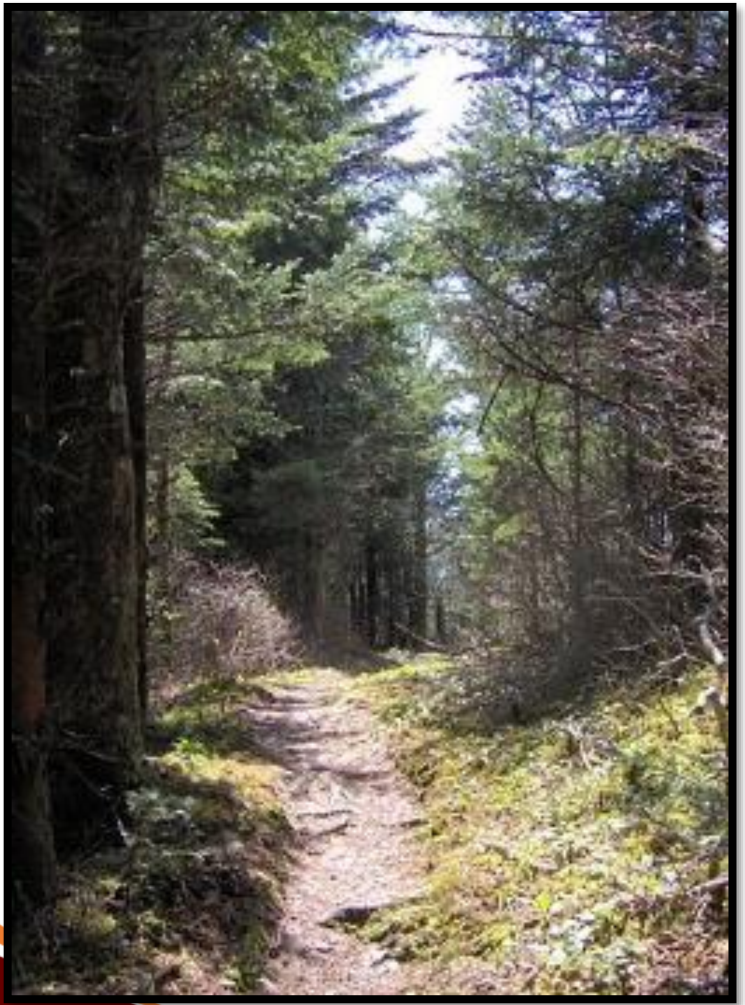
Check Methods

Some Helpful Hints…

- Read papers thoroughly
- Keep a pdf copy of all papers and update citations as you go
- Consider exclusion and inclusion criteria carefully

- Take a listing of papers provided by an external party without vetting
- Exclude papers unless you have to

Conducting the Analysis



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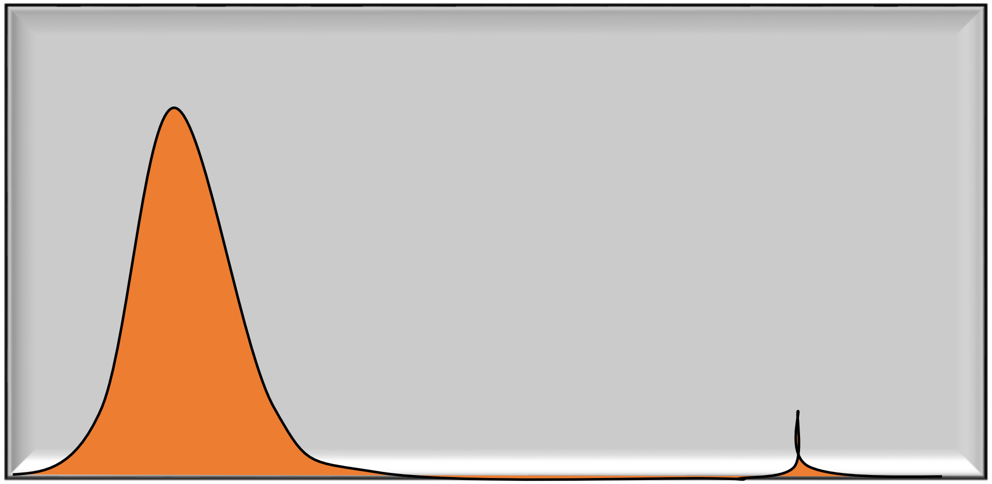
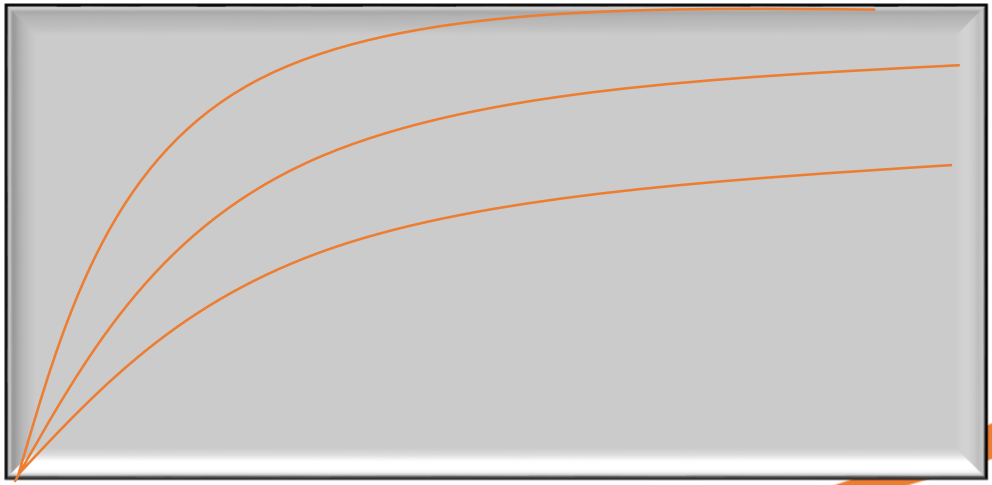
Conducting the Analysis

- **Visualize Data and Relationships**
- Calculate Weights
- Derive Model (Phase I)
- Re-test Dropped Parameters
- Perform Model Checks





Conducting the Analysis

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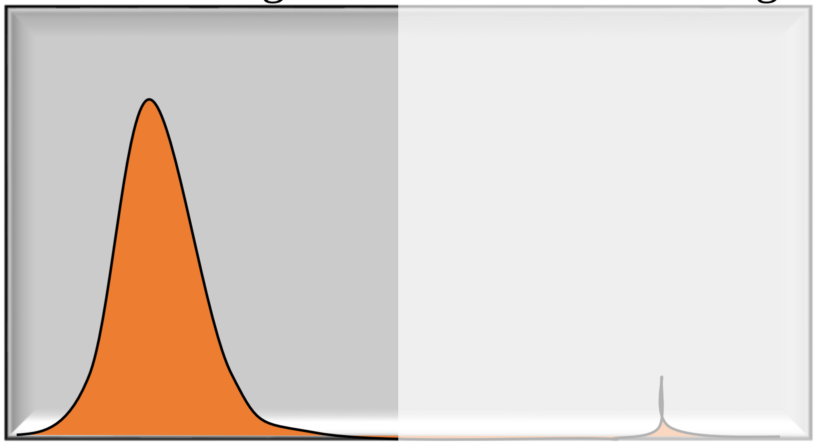
$$Weight = \frac{1}{SE} \; OR \; \frac{1}{SE^2}$$

Standard Errors from Mixed Effects Models are NOT Equal to Those From Fixed Effects Models

$$Standardized\ SE = \frac{SE}{\sum_{i=0}^{j} SE\ /n} \quad within\ model\ \ type$$

Weighting by $1/SE^2$ or failing to check the distribution of weights can result in overweighting.



Checking the distribution of weights and curtailing this distribution is a tool to prevent overweighting

Conducting the Analysis

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Protein Variables	AA Variables	Energy Variables
CP		
RUP		
		TDN Intake
	Absorbed Leu	
		NDF, % DM
	Absorbed Met	Starch, % DM

Conducting the Analysis

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Conducting the Analysis

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- Check variance inflation factors for parameters
- Evaluate and compare models
- Cross validate models

Variance Inflation Factors

The degree to which variance of a regression coefficient is inflated because of multicollinearity

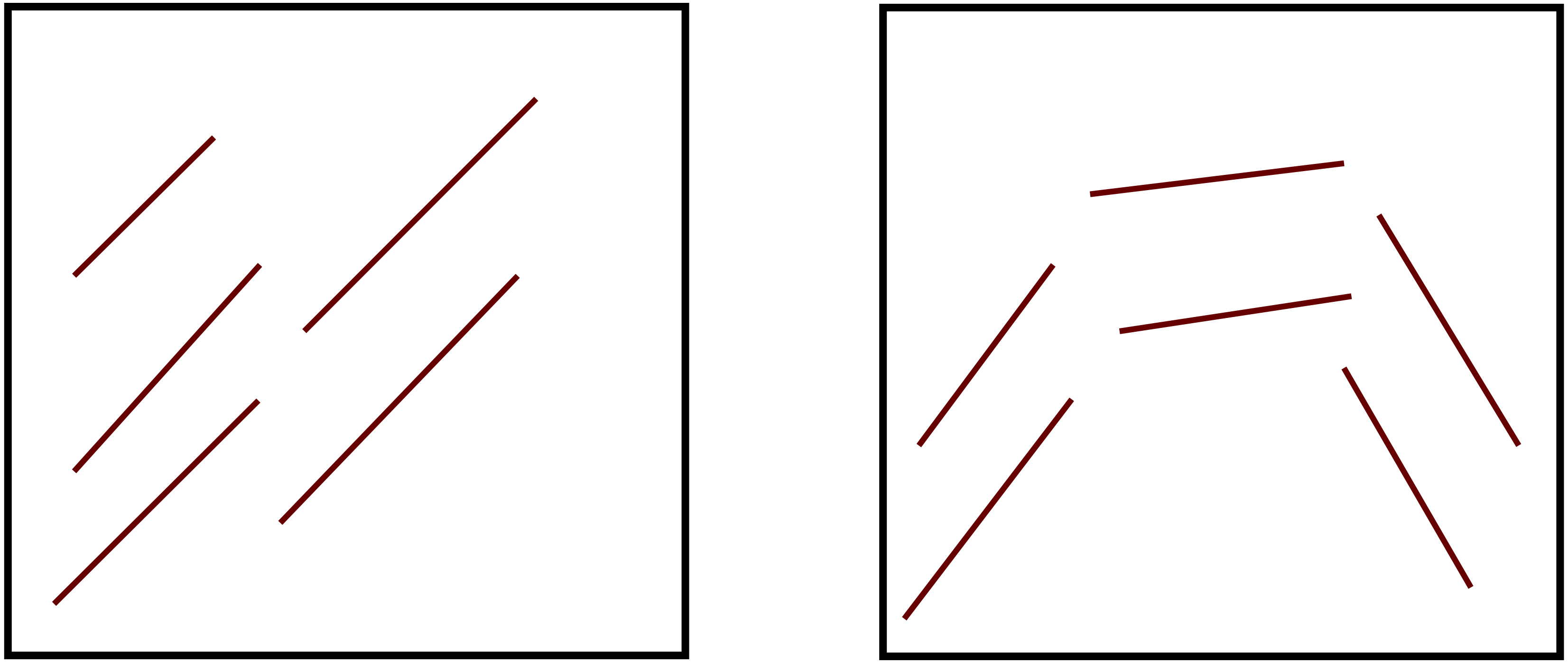
$$VIF_k = \frac{1}{1 - R_k^2}$$

Where R_k^2 is the R^2 obtained by regressing predictor "k" on the other predictors

No "set in stone" cutoff; however, published papers have used 5, 10, or up to 100 for variables anticipated to be correlated by calculation

Slope by Study Interactions

Check and attempt to eliminate slope by study interactions

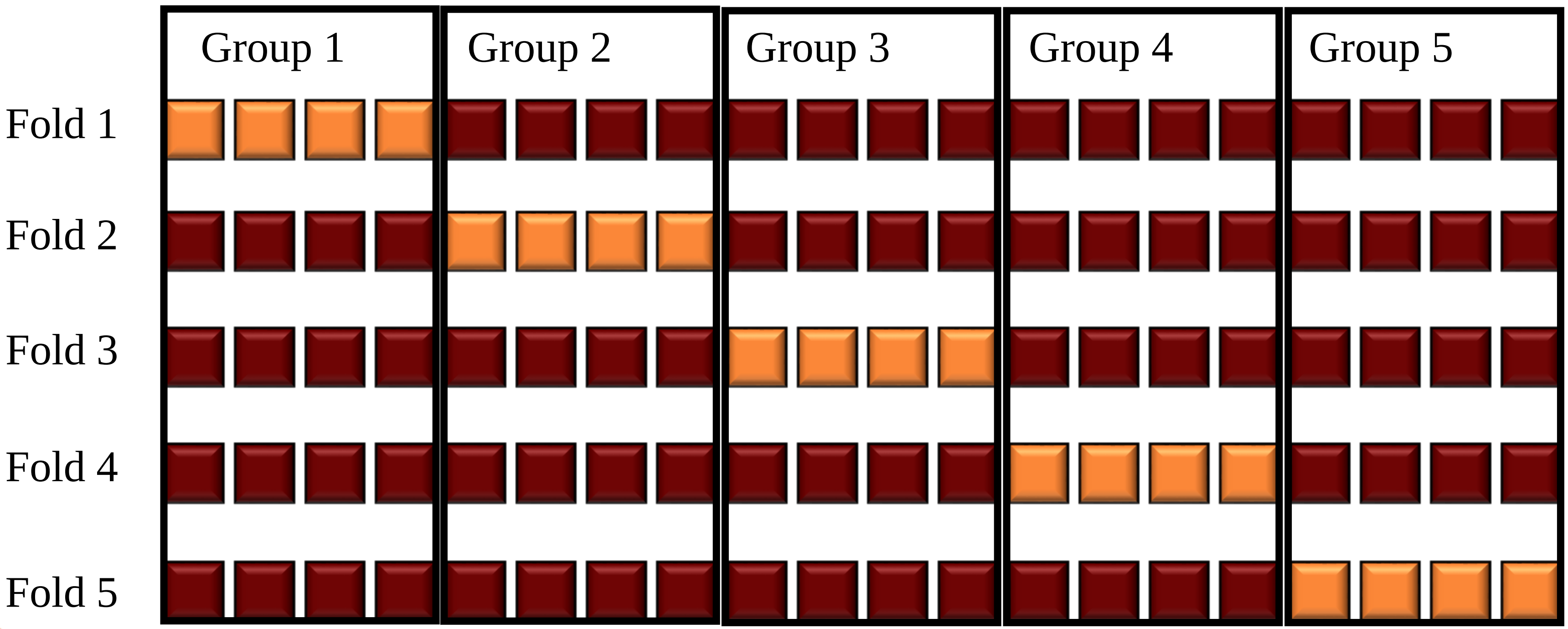


Evaluating and Comparing Models

Statistic	Notes
AICc	Gold standard for comparing models but can only be interpreted if derivation data is identical among models.
RMSE	Standard comparison for models derived using least-squares approaches.
Slope bias	Represents structural issues in a model. The errors scale with the magnitude of the prediction.
Mean bias	Represents an "average" error in the model. All predictions are off by some value.
CCC	Represents the concordance (accuracy and precision) of measured and modeled data.
σ_s	Root estimated variance associated with study.
σ_e	Root estimated error variance. Equivalent to an RMSE for models derived using maximum likelihood.

Cross Validation

K-Fold Cross Validation: Split the data into "k" groups and iterate through model derivation and testing so that each group is used for model testing exactly once.



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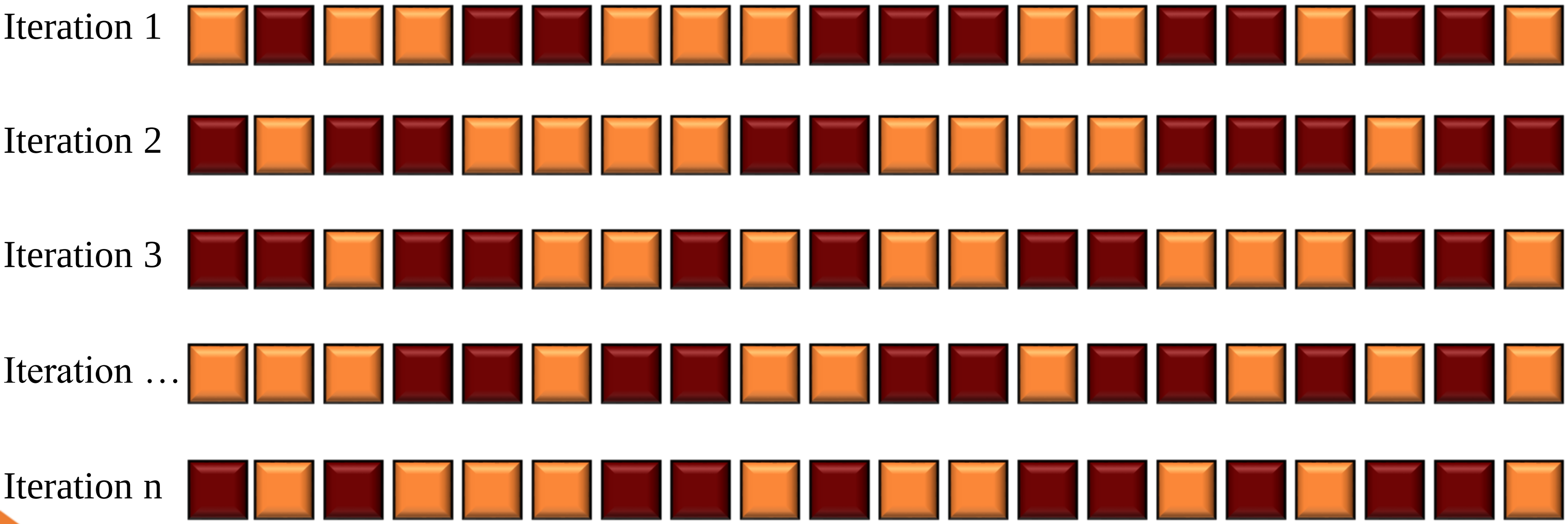
Cross Validation

Monte Carlo Cross Validation: Split the data into 2 groups of user-determined size derive the model against group 1 and test against group 2. Repeat "n" times.



Questions?

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