

Medical Epistemology (A Gerontologist's Perspective)

John Sorkin, M.D. Ph.D.
Chief, Biostatistics,
Baltimore VAMC GRECC,
UM Claude D. Pepper Older Americans Independence
Center,
U. Maryland Clinical Nutrition Research Unit and
Baltimore VA Med. Center of Excellence in Robotics and
Stroke Rehabilitation

Dedication

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- A room should be named in her honor!

Gerontology and Aging

- Questions
 - What are the aims of gerontology?
 - What is aging?

Gerontology and Aging

- Questions
 - What are the aims of gerontology?
 - What is aging?

 - How do we know what we “know”?

Gerontology – A few Aims

- To identify changes that occur with aging
- To quantify the rate at which change occurs
- To understand the mechanisms behind the changes

Aging is the result of

- Intrinsic biological process that are genetically determined (biological aging)
- Age-associated life style changes
 - Decreased physical activity
 - Increased obesity
- Age-associated increased incidence and prevalence of disease

Aims of this presentation

- To describe three study designs
 - Cross-sectional
 - Time-series
 - Longitudinal

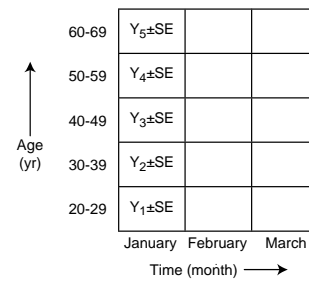
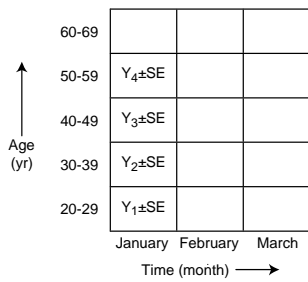
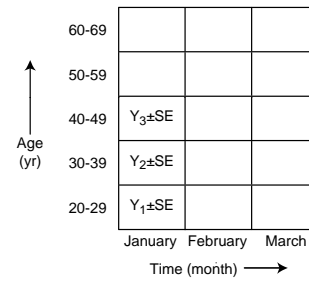
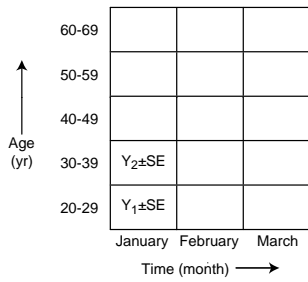
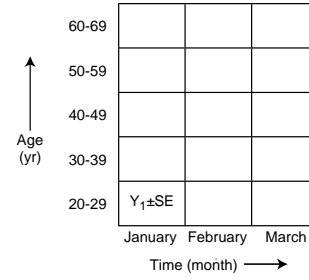
Aims of this presentation

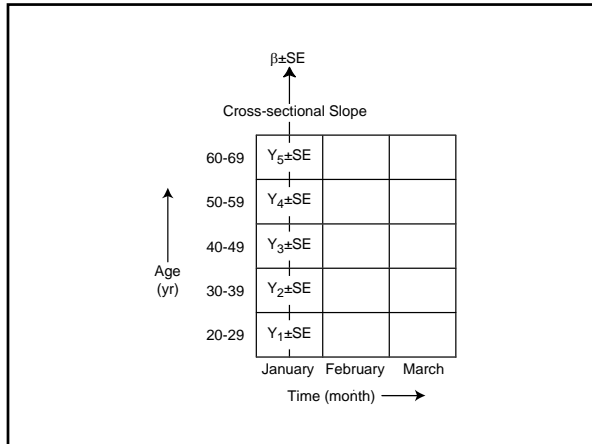
- Study designs that can be used to
 - Identify change
 - Quantify the rate at which change occurs at different ages
 - Separate biological aging (primary aging) from the effects of
 - Life style (secondary aging) and
 - Disease (tertiary aging)

Aims of this presentation

- To describe problems and limitations associated with the three study designs
- To review techniques that inform us about the process of aging
 - Strengths
 - Weaknesses

Cross-Sectional Design



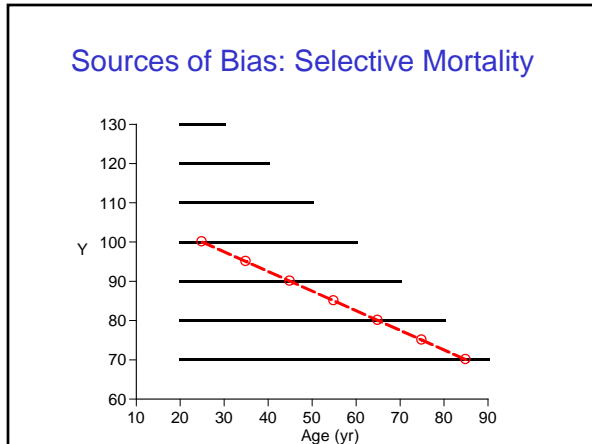
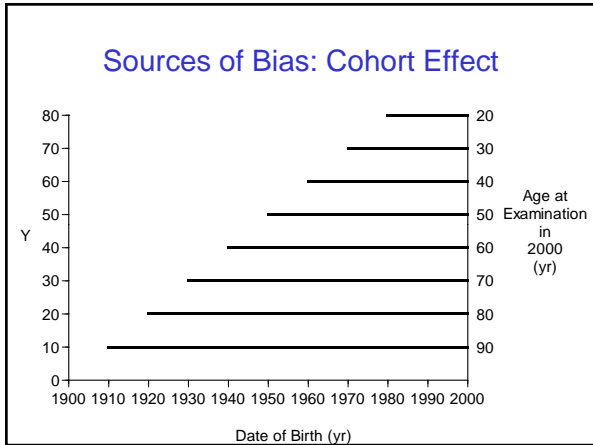


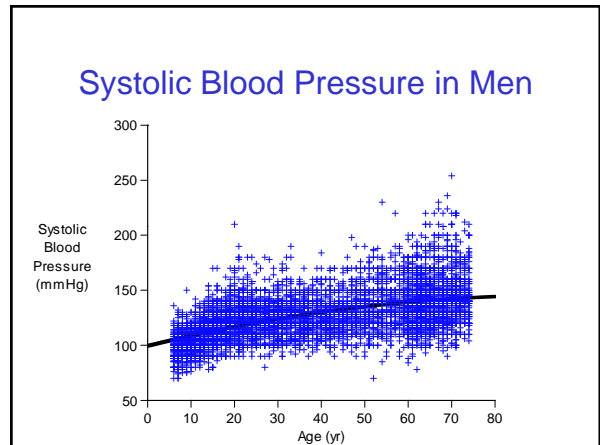
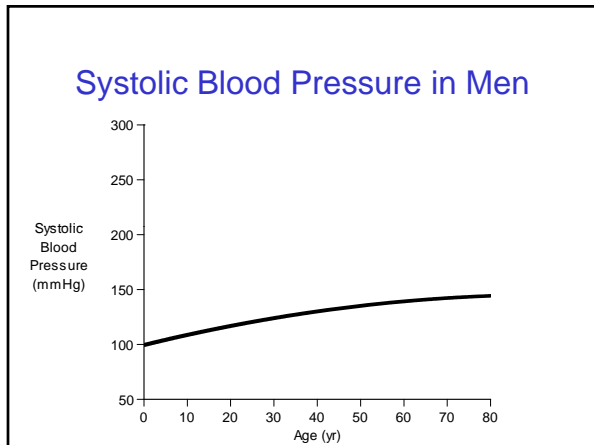
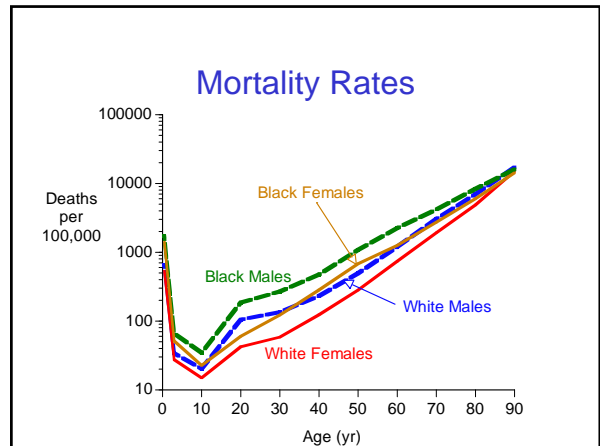
Sources of Bias: Cross-Sectional Study Cohort Effect

- A cross-sectional study finds height decreases with age
 - Etiologies
 - Loss of height due to disc shrinkage and loss of spinal bone mineral density
 - OR
 - Birth cohort effect

Cohort Effect (or Generational Effect)

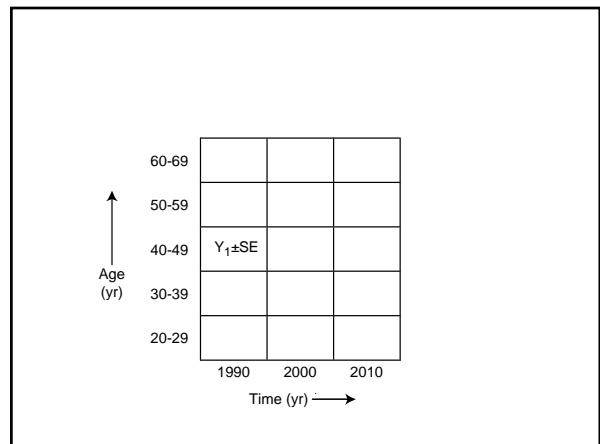
- A variation in health status that arises from the different factors to which each birth cohort is exposed as the environment and society changes
 - E.g. Nutrition in-utero and childhood can affect height

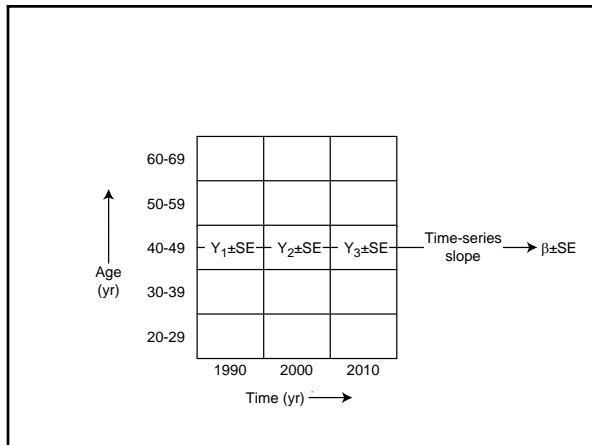
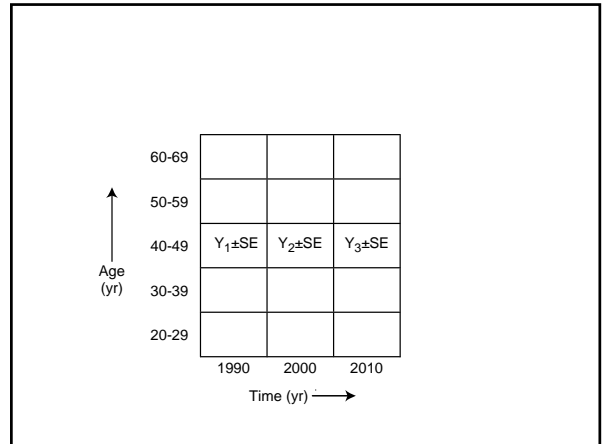
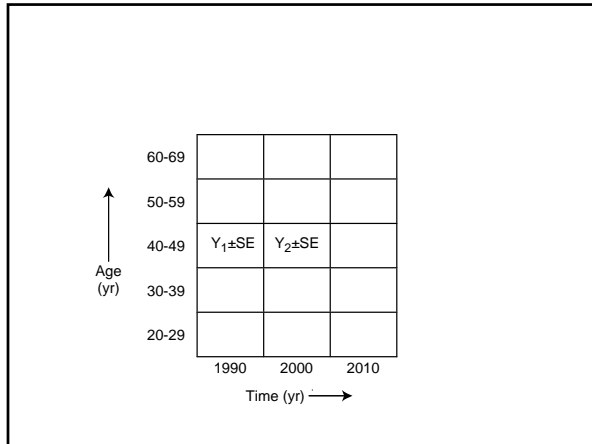




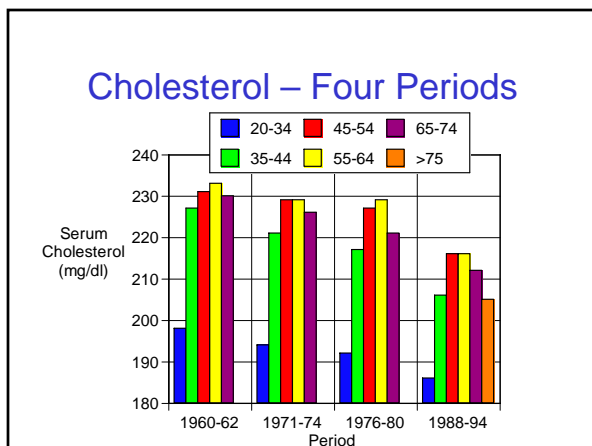
Time-Series Design

- Confusing terminology
 - Panel Study

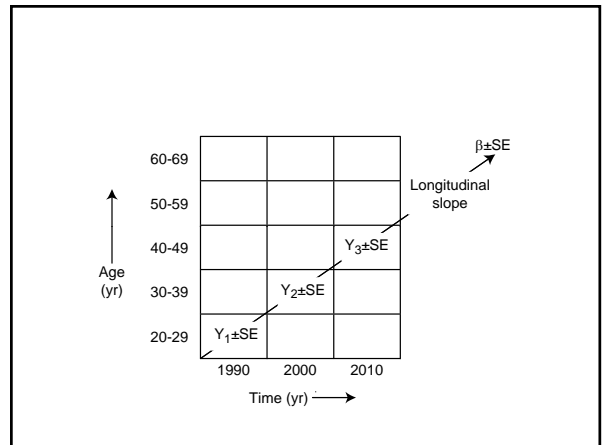
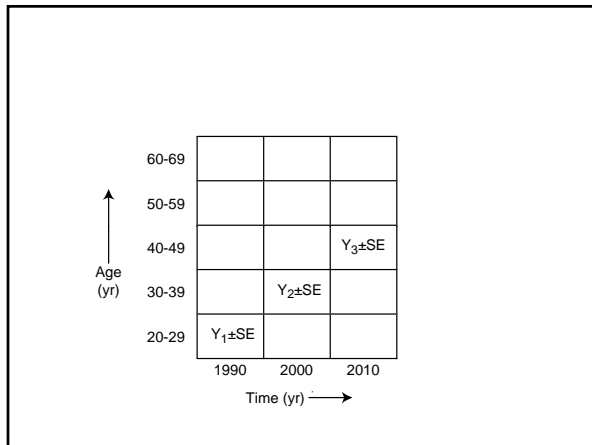
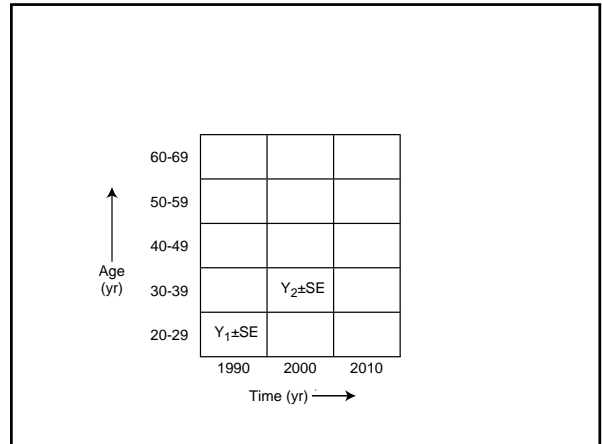
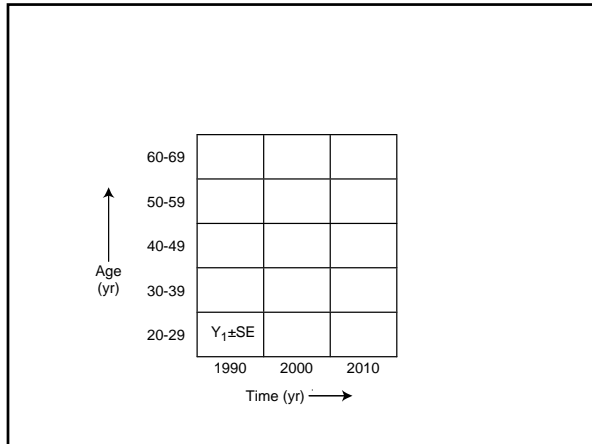




- ### Sources of Bias: Time-series Analyses Selection Bias
- Selection Bias
 - Consider a study of height
 - Study Lilliputians in 1980
 - Study Giants in 2000
 - Methodologic change
 - Consider a serum cholesterol
 - Use one instrument in 1980
 - Use another instrument in 2000



Longitudinal Design

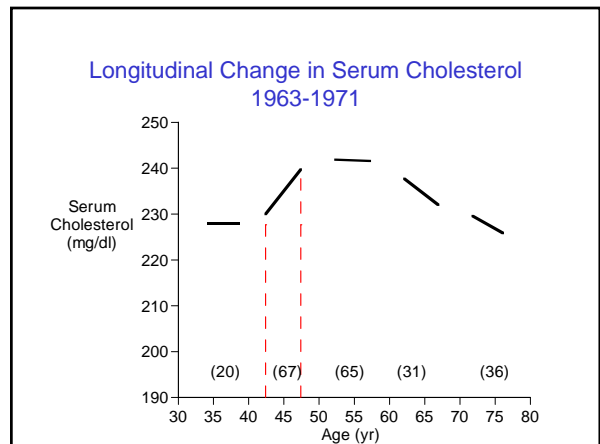
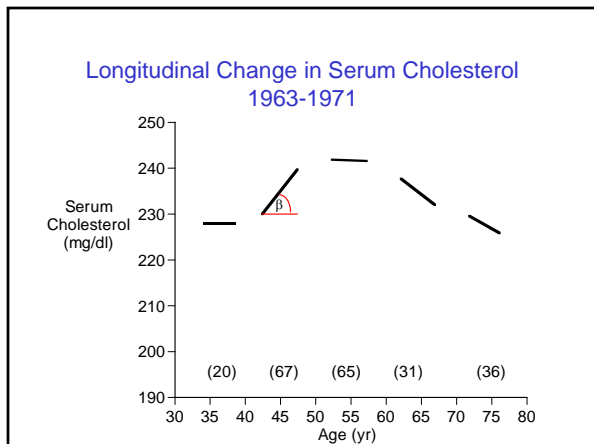
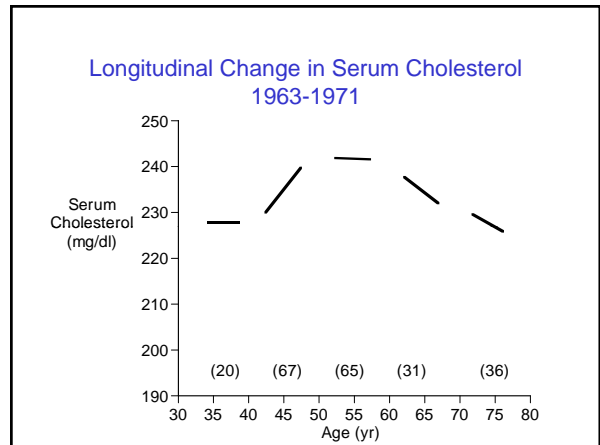
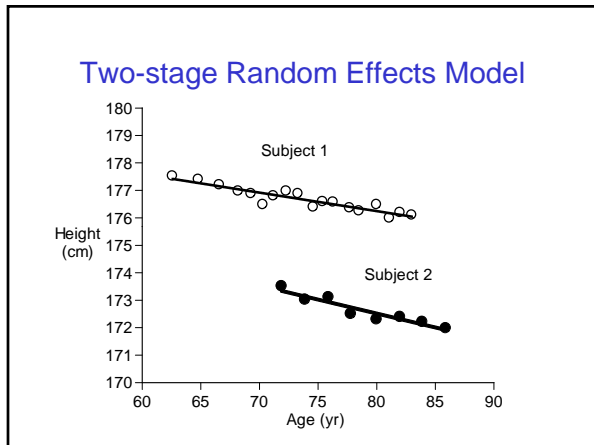
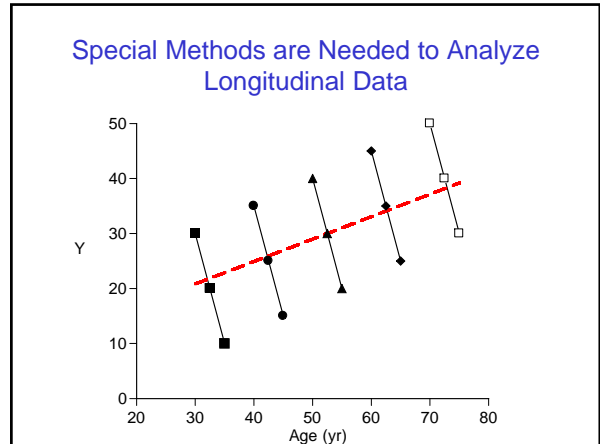
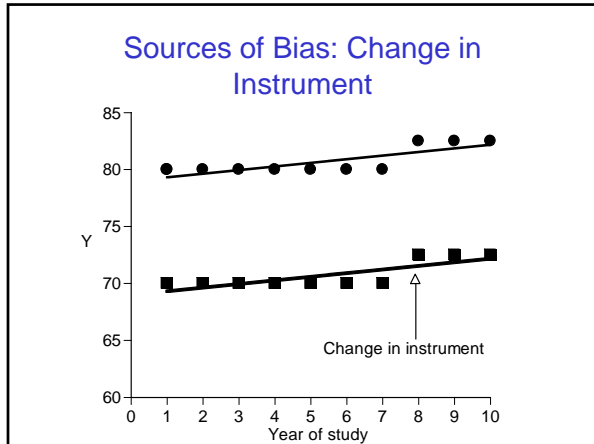


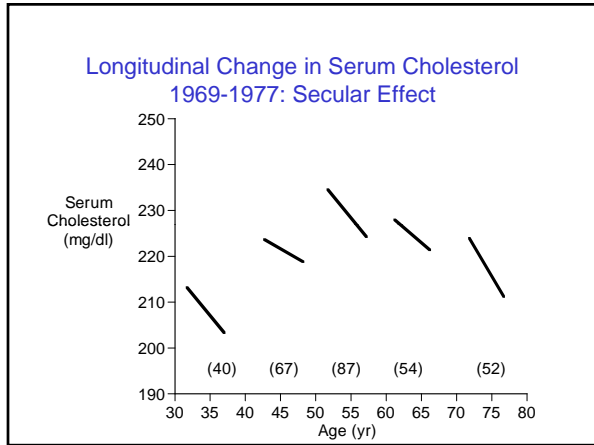
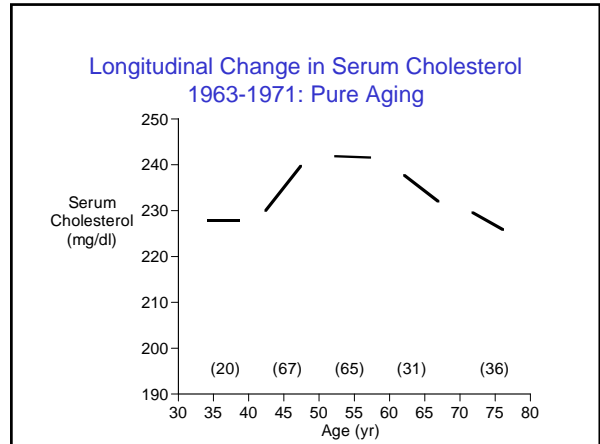
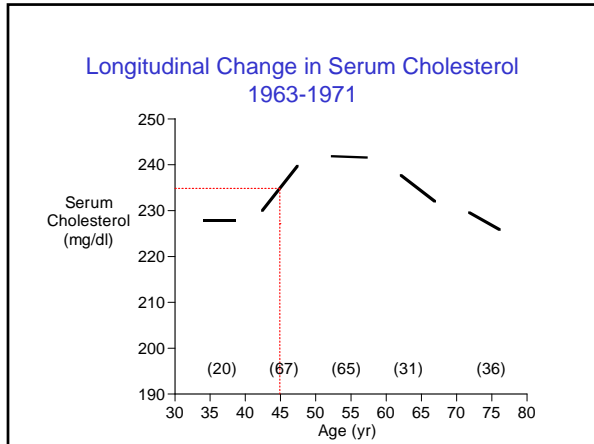
Sources of Bias: Longitudinal Study
Secular Trend

- A longitudinal study finds a fall in serum cholesterol with aging
 - Etiologies
 - True change in metabolism with aging
 - OR
 - **Secular trend**

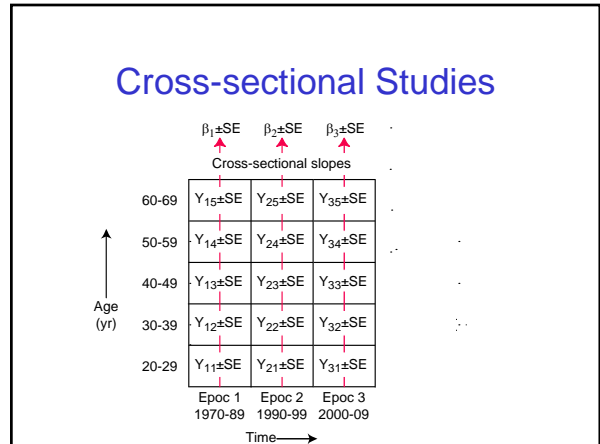
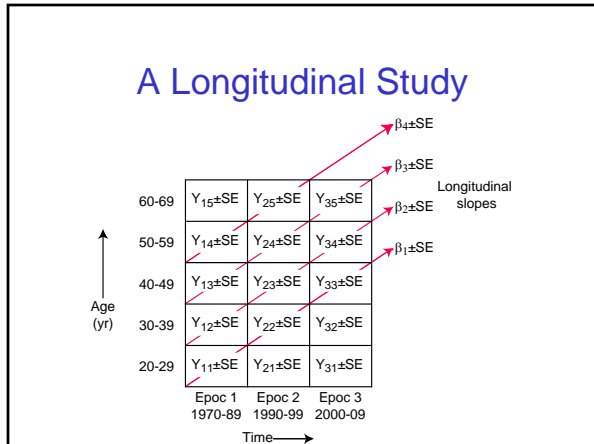
Secular Trend
(or Temporal Trend)

- A change occurring over a long time period, often years or decades that is the result of environmental influences rather than primary (biological) aging.
- E.g. As society slowly accepts that elevated cholesterol concentration leads to heart disease, people eat less fat and cholesterol concentrations drop.

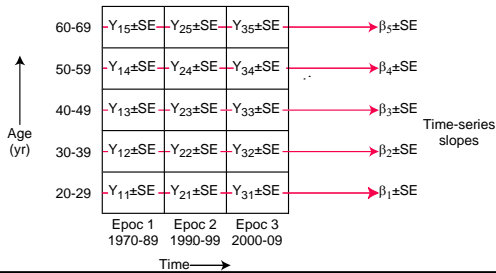




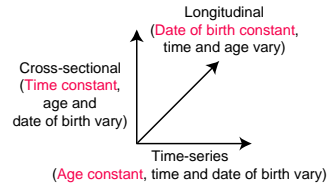
Identifying Aging, Secular, and Cohort Effects



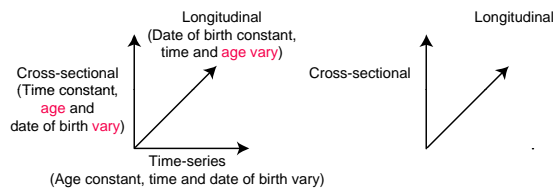
Time-series Studies



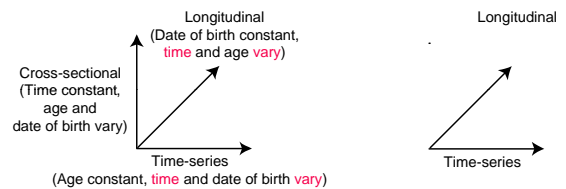
Characteristics of Study Designs



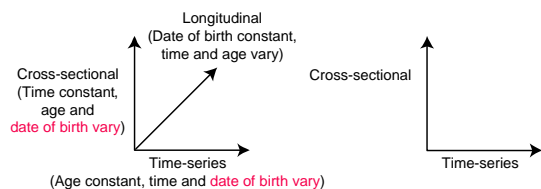
Pure Aging Effect Age Varies



Pure Secular Effect Time Varies



Pure Cohort Effect Date of Birth Varies



Advantages of Cross-Sectional Design

- Can be performed **quickly**
- Relatively **Inexpensive**

Disadvantages of Cross-Sectional Design

- Suffer from **recall and assignment bias**
- Can not establish **temporal association**

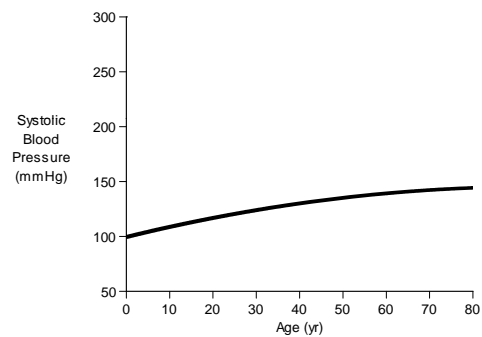
Disadvantages of Longitudinal Design

- **Take years** to perform
- **Expensive**
- Sensitive to **change in measurement**
- Subject to bias due to **loss to follow-up**

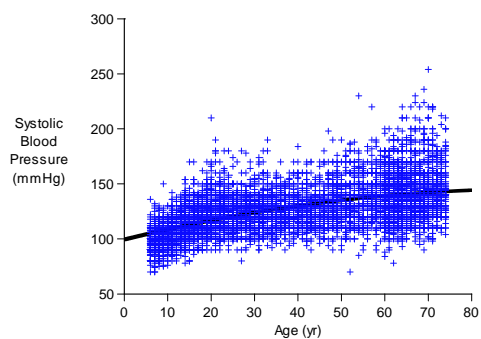
Advantages of Longitudinal Design

- **Do not suffer** from selective mortality or cohort effects
- **Can establish** temporal association

Systolic Blood Pressure in Men



Systolic Blood Pressure in Men



Important Caveat

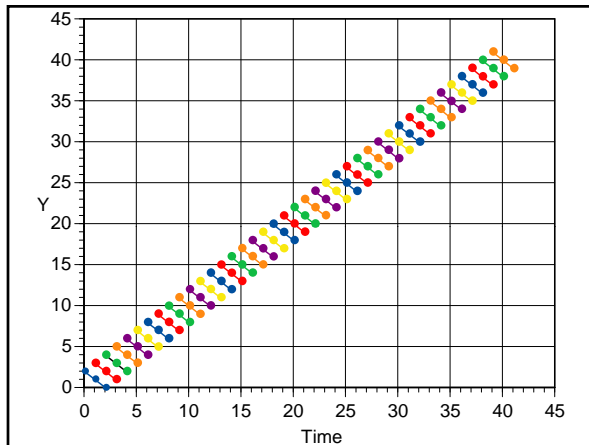
- **Regardless of design**
 - Summary data from
 - Cross-sectional
 - Time-series
 - Longitudinal

Important Caveat

- Regardless of design
 - Summary data from
 - Cross-sectional
 - Time-series
 - Longitudinal
 - May mask important between individual differences

Four Techniques for Analyzing Longitudinal Data

An Aperitif



Four Regression Strategies

- Standard regression
- GEE (General Estimating Equations)
- Two-stage random effects regression
- Random effects regression

Four Regression Strategies

- Ignores data come from multiple subjects
 - Standard regression
- Considers data come from multiple subjects
 - GEE (General Estimating Equations)
 - Two-stage random effects regression
 - Random effects regression

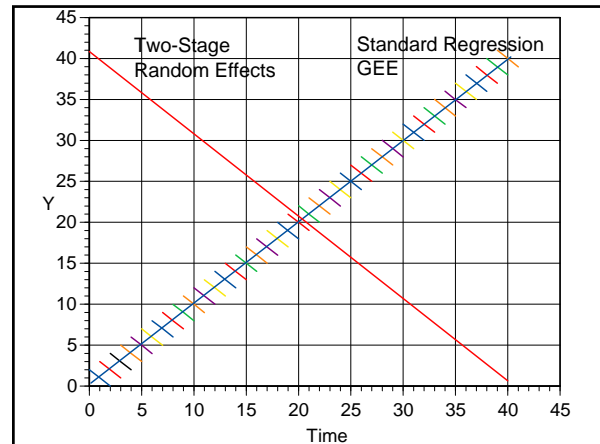
Four Regression Strategies

- Ignores data come from multiple subjects
 - Standard regression
- Considers that data come from multiple subjects
 - GEE (General Estimating Equations)
 - Marginal model
 - Two-stage random effects regression
 - Analysis done in two steps
 - Random effects regression
 - Analysis done in a single step

Comparison of Results

Model	Parameter	Estimate			Precision*	
		β	SE	p	Absolute	Relative
Standard regression	Intercept	0.4	0.44	0.35	2	1
GEE		0.0	0.00	0.95	18	12
Random effects regression	Two-state random effects	21.0	2.65	0.00	1	0.4
Two-state random effects		21.0	2.65	0.00	1	0.4
Standard regression	Time	1.0	0.04	0.00	5	1
GEE		1.0	0.00	0.00	68	13
Random effects regression	Two-state random effects	-1.0	0.00	0.00	24	5
Two-state random effects		-1.0	0.00	0.00	24	5

* 1/variance; Larger is better



Epistemology

- The branch of philosophy dealing with the origin, nature, and limits of knowledge.

Standard Regression

```
proc reg data=in2;
  title "Standard regression ignoring subject";
  model y=time;
run;
```

GEE

```
proc genmod data=in2;
  title "GEE";
  class Subject;
  model y = time / type3;
  repeated subject=subject / type=exch covb corrw;
run;
```

Two-Stage Random Effects Regression

```
ods output ParameterEstimates=PE (keep=subject variable estimate);
proc reg data=in2;
  title "Two-stage random effects: Subject by subject regression";
  by subject;
  model y=time;
run;
title;
ods output close;
```

Two-Stage Random Effects Regression

```
proc means data=PE n mean var stddev stderr min
max probt t;
  title "Two-stage random effects mean of
parameter estimates.";
  class variable;
  var estimate;
  output out=means mean=estimate stderr=stderr
t=tvalue probt=p;
run;
title;
```

Random Effects Regression

```
proc mixed data=in2;
  title "Random effects regression";
  class subject;
  model y=time/solution;
  random intercept /type=un subject=subject;
  * Initial estimates for variance intercept,
variance slope.;
  *These parameters are needed to allow
convergence;
  parms (546) (1);
run;
```