WHY MODEL?
AN INTRODUCTION TO MODELING

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Learning objectives
At the end of this lecture you will be able to

- Explain what a model is
- Explain why models are used in research
- Describe the most commonly used models

- Key concepts
  - Estimand, estimator, estimate
  - Consistent estimator
  - Parametric and nonparametric estimators
  - Linear and logistic regression

Plan for today

A. The need for models: A motivation

B. Types of models frequently used in epidemiology

C. Linear regression and logistic regression

A. The need for models: A noncausal motivation

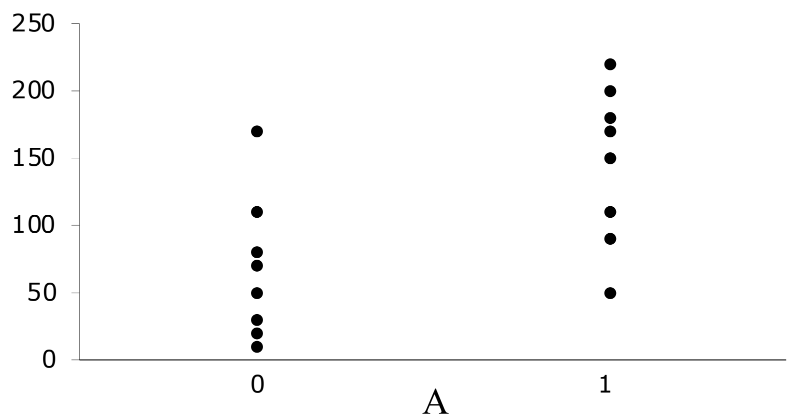
- Consider the following study
- Study population: 16 individuals living with HIV
  - Not 16,000 or 16 million
- Predictor: antiretroviral therapy A
  - Each individual receives certain level a
- Outcome: CD4 cell count at the end of follow-up Y
  - A continuous variable

Goal of our predictive analysis

- To estimate the mean of Y among individuals with treatment level $A=a$ in the population from which these individuals were randomly sampled

- This conditional population mean is represented as $E[Y|A=a]$
  - Expected value of Y given (among those with) treatment A equal to a

Dichotomous predictor



Your best estimate of the mean outcome in those receiving A=1 in the population?

0

(A) 200 — 0%

(B) 150 — 0%

(C) 100 — 0%

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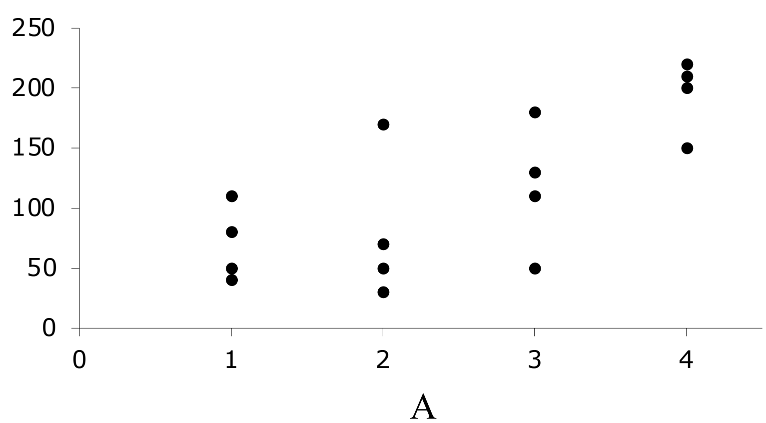
Estimand, Estimator, Estimate

- The estimand is the unknown population parameter
  - The mean of Y among those with $A=1$ in the population
- An estimator is some function of the data that is used to estimate the estimand
  - The sample average of Y among those with $A=1$
- An estimate is the result of applying the estimator to a particular data set
  - 146.25

A consistent estimator

- "The larger the sample size, the closer the sample estimate to the population estimand"
  - Formally: an estimator provides a consistent estimate $\hat{\mathrm{E}}[Y|A=a]$ of the estimand $\mathrm{E}[Y|A=a]$ if the difference $\hat{\mathrm{E}}[Y|A=a] - \mathrm{E}[Y|A=a]$ approaches zero as the sample size increases towards infinity
  - The hat ^ commonly used to refer to estimates
- Examples:
  - Consistent estimator of the population mean: the sample average
  - Inconsistent estimator of the population mean: the value of the first observation in the data
- We require that estimators be consistent

Polytomous predictor



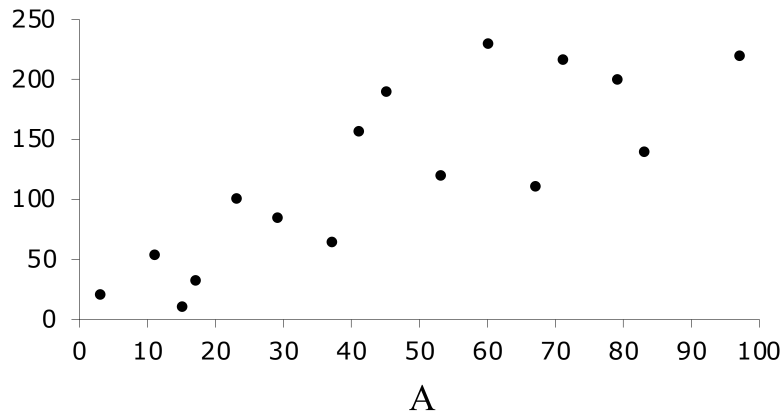
Your best estimate of the mean outcome in those receiving A=4 in the population? 0

200	**0%**
150	**0%**
100	**0%**

Discrete predictor (dichotomous or polytomous)

- As the number of categories increase, the number of individuals per category decreases
  - Variance increases
- But the sample average is still a consistent estimator of the population mean
  - The average of Y in each level of A in our sample consistently estimates the mean of Y in each level of A in the population

Continuous predictor



Your best estimate of the mean outcome in those receiving A=50 in the population? 0

200 **0%**

150 **0%**

100 **0%**

Continuous predictor

- Conceptually, a categorical variable with an infinite number of categories
  - What if there are no individuals with treatment value $A=a$?
  - Cannot use the average of Y in each level of A
- In general, it is impossible to consistently estimate $\mathrm{E}[Y|A=a]$ by using the data only
- We need to supply additional information
  - A priori knowledge that is not in the data

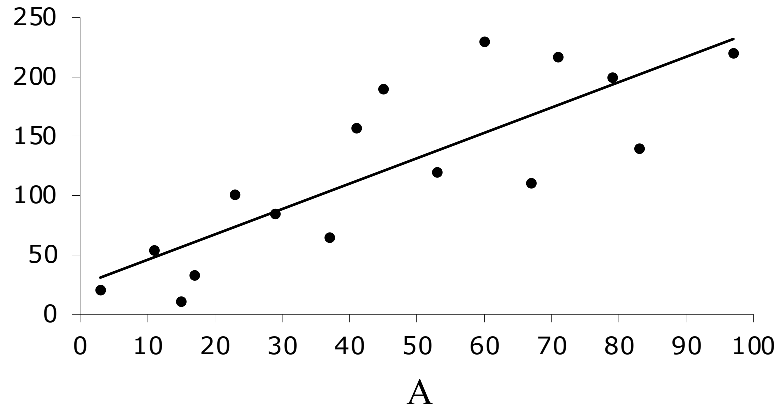
An example of a priori information

- The mean of Y follows a straight line
  - the mean of Y is directly proportional to the value of A
  - The mean of Y is θ_0 when $A=0$, and increases (or decreases) by θ_1 units per unit of A
- Or, more compactly,

  $\mathrm{E}[Y|A]= \mathrm{E}[Y|A=0] + \theta_1 A = \theta_0 + \theta_1 A$
  - θ_0 is known as the intercept
  - θ_1 is known as the slope

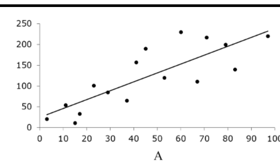
A linear model

$E[Y|A] = \theta_0 + \theta_1 A$



A linear model

$E[Y|A] = \theta_0 + \theta_1 A$



- The parameters θ_0 and θ_1 are consistently estimated by ordinary least squares estimation
- Find the line that results in the minimum sum of squared differences between each point and the straight line
  - θ_0 is estimated as the point at which the line crosses (intercepts) the vertical axis
  - θ_1 is estimated as the slope of the line

Smoothing with a linear model

$E[Y|A] = \theta_0 + \theta_1 A$

- One can use the estimates of θ_0 and θ_1 to predict the mean of Y for any possible value $A=a$, including those values not present in the data

- The mean of Y in those with $A=a$, i.e., $E[Y|A=a]$ is estimated by borrowing information from individuals with A not equal to a
  - Because ordinary least squares estimation uses all data points to find the best line

Definition of Model: a restriction on the possible values of the quantity of interest

- Consider our linear model for the conditional mean

$$E[Y|A] = \theta_0 + \theta_1 A$$

  - the mean of Y for $A=50$ cannot take any value
  - It is restricted to be in between the mean of Y for $A=40$ and the mean of Y for $A=60$
  - The restriction is encoded by parameters like θ_0, θ_1

- How do we choose the restrictions of the model?
  - Using a priori knowledge, if available, or
  - Making unverifiable (modeling) assumptions

Parametric and nonparametric estimators

- Nonparametric estimators
  - Use ONLY the data
  - Do not impose a priori restrictions on the value of the estimate
  - Example: the sample average
- Parametric estimators
  - Use the data plus a priori restrictions on the value of the estimate
  - Example: the above linear model

Nonparametric models: not really models

- No a priori restrictions because they have
  - as many parameters as quantities the model can estimate
  - also known as saturated models
- Example: for a dichotomous treatment

$$\mathrm{E}[Y|A] = \theta_0 + \theta_1 A$$

  is not really a model
  - Just says that $\mathrm{E}[Y|A=1]$ is equal to $\mathrm{E}[Y|A=0]$ plus a quantity θ_1, which is of course always true, so there is no restriction

High dimensionality: multiple covariates

- Estimate the mean $E[Y|A=a, L=l]$ in the presence of a vector of 20 covariates L
  - Number of strata grows exponentially, much faster than number of individuals
  - e.g., if 20 dichotomous covariates, there are 2^{20} (approx 1 million) possible combinations per treatment value
  - The curse of dimensionality
- Nonparametric estimators unfeasible
- Models are our only hope in high-dimensional settings

The price of modeling

- Models allow us to estimate quantities that cannot be nonparametrically consistently estimated
- But not a free lunch
  - Parametric inference correct only if the model is correctly specified
  - Model specification can be empirically checked only to some extent
- Causal inference with models requires the condition of no model misspecification

Plan for today

A. The need for models: A motivation

B. Types of models frequently used in epidemiology

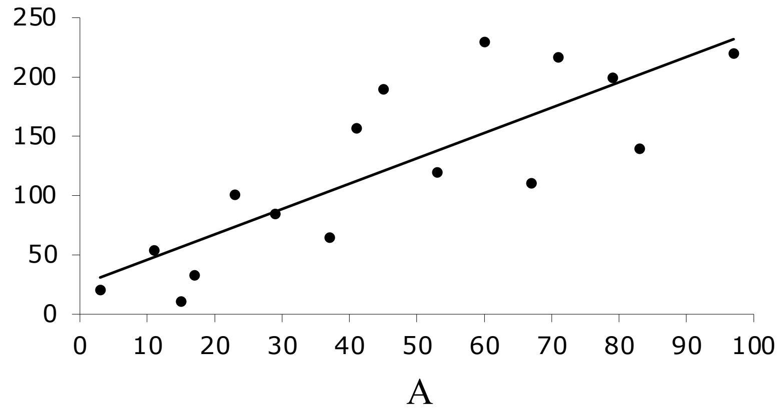
C. Linear regression and logistic regression

B. Models frequently used in epidemiology

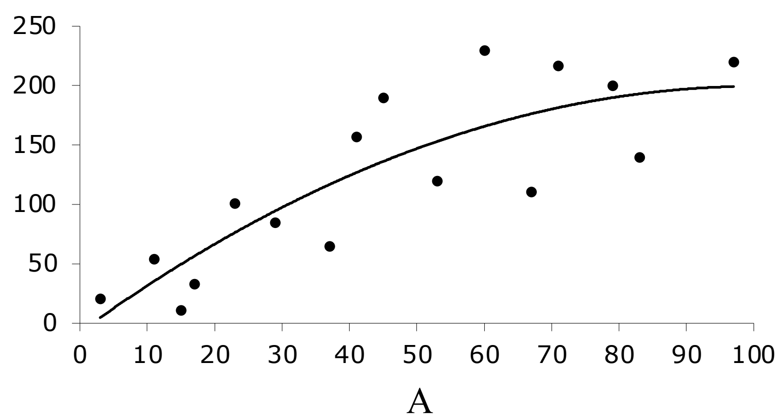
- ☐ Linear models
- ☐ Generalized linear models
- ☐ Generalized additive models
- ☐ Models for survival analysis

➢ Known as regression models

A linear model
$E[Y|A]= \theta_0 + \theta_1 A$

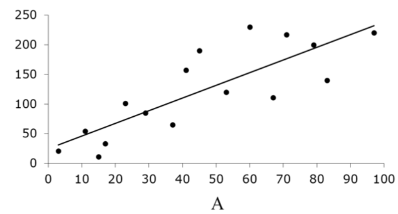


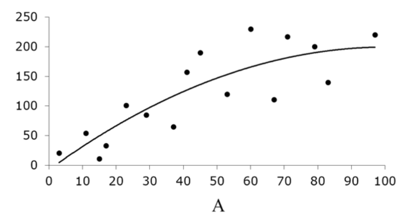
Another linear model
$E[Y|A]= \theta_0 + \theta_1 A+ \theta_2 A^2$



We need to decide which model to use to estimate $\mathrm{E}[Y|A]$

- Problem: we don't know what the true relation between A and Y is
  - a straight line or a curve?
- If we knew the shape of the true relation, it'd be easy to decide. Right?





If the true relation is a straight line, will the model $E[Y|A] = \theta_0 + \theta_1 A$ estimate $E[Y|A]$ correctly?

Yes — **0%**

No — **0%**

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If the true relation is a straight line, will the model $E[Y|A] = \theta_0 + \theta_1 A + \theta_2 A^2$ estimate $E[Y|A]$ correctly?

Yes 0%

No 0%

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If the true relation is a quadratic curve, will the model $E[Y|A] = \theta_0 + \theta_1 A$ estimate $E[Y|A]$ correctly?

0

Yes 0%

No 0%

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Which linear model imposes more restrictions on (makes more assumptions about) the true relation?

The straight line

0%

The quadratic curve

0%

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Generalized linear models Examples

- Linear
  - Means

$$E[Y|A] = \theta_0 + \theta_1 A$$

- Log-linear
  - Counts *N*
  - Rates N/PT (PT: person-time)
    - $\ln(N/\mathrm{PT}|A) = \theta_0 + \theta_1 A$
    - $\ln(N|A) = \theta_0 + \theta_1 A + \ln(\mathrm{PT}|A)$

$$\ln(E[Y|A]) = \theta_0 + \theta_1 A$$

- Logistic
  - Proportions
  - $E[Y|A=a]=\Pr[Y=1|A=a]$

$$\mathrm{logit}(E[Y|A]) = \theta_0 + \theta_1 A$$

Extensions of generalized linear models

- Generalized linear models assume
  - a functional form
    - e.g., a linear combination of parameters and covariates
  - a statistical distribution
    - e.g., errors are independent and normally distributed with mean zero and constant variance
- Generalized linear models may relax the statistical assumptions for longitudinal data
  - GEE (generalized estimating equations) models
  - Random effects/Mixed effects models

Generalized additive models

- Like generalized linear models but they replace the linear function of covariates by a sum of functions of the covariates
  - Examples of functions: moving average, locally-weighted running mean
- $E[Y|A=a]$ may be estimated by borrowing information from some, but not all, individuals with A not equal to a
  - More "nonparametric", varying degrees of smoothing

Models for survival (failure time) data

- Need to accommodate censoring
- Parametric
  - Exponential
  - Weibull
- Semiparametric
  - Cox proportional hazards model
  - Accelerated failure time model
  - Baseline hazard is unspecified (not restricted a priori)

Plan for today

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C. Linear and logistic regression

- Two types of general linear models

- Linear regression for continuous outcomes
  - e.g., blood pressure

- Logistic regression for dichotomous outcomes
  - e.g., death (1: yes, 0: no)

Linear regression

- Can be used to estimate the mean Y conditional on treatment A and covariates L
- For example
  - Y is weight gain
  - A smoking cessation (1: yes, 0: no)
  - L is age (in years)

- Consider the model $\mathrm{E}[Y|A,L]= \theta_0 + \theta_1 A + \theta_2 L$
  - Parameter estimates for θ_0, θ_1, θ_2 are obtained by ordinary least squares or maximum likelihood (see Biostatistics courses)

Interpretation of θ_0 (intercept) in $E[Y|A,L] = \theta_0 + \theta_1 A + \theta_2 L$?

Mean outcome when both A and L take value zero — **0%**

Difference in mean outcome between the strata A=1 and A=0, within levels of L — **0%**

Change in mean outcome per unit of L (‘year’ here), within levels of A — **0%**

Interpretation of θ_1 in $E[Y|A,L] = \theta_0 + \theta_1 A + \theta_2 L$?

Mean outcome when both A and L take value zero — **0%**

Difference in mean outcome between the strata A=1 and A=0, within levels of L — **0%**

Change in mean outcome per unit of L (‘year’ here), within levels of A — **0%**

Interpretation of θ_2 in $E[Y|A,L] = \theta_0 + \theta_1 A + \theta_2 L$?

Mean outcome when both A and L take value zero

0%

Difference in mean outcome between the strata A=1 and A=0, within levels of L

0%

Change in mean outcome per unit of L ('year' here), within levels of A

0%

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Predicted values
$\hat{E}[Y|A=a, L=l]$

- The estimates of $E[Y|A=a, L=l]$ for each combination of values of treatment $A=a$ and covariates $L=l$
  - Obtained by replacing the parameters θ_0, θ_1, θ_2 by their estimates $\hat{\theta}_0$, $\hat{\theta}_1$, $\hat{\theta}_2$
  - Example:
    - for treated individuals aged 30 years, the predicted value is
    - $\hat{E}[Y|A=a, L=l] = \hat{\theta}_0 + \hat{\theta}_1 \times 1 + \hat{\theta}_2 \times 30$
  - Residual: the difference between an individual's value of Y and the predicted value $\hat{E}[Y|A=a, L=l]$ for their combination of values of A and L

Logistic regression

- Can be used to estimate the probability of an event D conditional on treatment A and covariates L
- Consider the logistic model

$$\text{logit}\ \Pr[D=1|A,L]= \theta_0 + \theta_1 A+ \theta_2 L$$

  - D is death (1: yes, 0: no)
  - A is smoking cessation (1: yes, 0: no)
  - L is age (in years)

Interpretation of θ_1 in $logitPr[D=1|A,L]=\theta_0+\theta_1 A+\theta_2 L$?

log risk ratio of D for A=1 compared with A=0, within levels of L — 0%

log odds ratio of D for A=1 compared with A=0, within levels of L — 0%

Neither of the above — 0%

See Homework #1

- For a detailed interpretation of the parameters of logistic models and a description of the logit function

- See Biostatistics courses
  - For a description of maximum likelihood estimation to obtain parameters estimates for θ_0, θ_1, θ_2

Predicted values

- The estimates of $\text{logit}\Pr[D=1|A=a, L=l]$ for each combination of values of treatment $A=a$ and covariates $L=l$
  - Obtained by replacing the parameters θ_0, θ_1, θ_2 by their estimates $\hat{\theta}_0$, $\hat{\theta}_1$, $\hat{\theta}_2$

- To get the probability $\Pr[D=1|A=a, L=l]$ rather than the logit of the probability, we need to do some algebra
  - In practice, computers do it for us
  - You will do it yourself in Homework #1

Why logistic regression for dichotomous outcomes?

- Because the logit transformation ensures that the predicted values will always be between 0 and 1
  - regardless of the values of the parameter estimates and the covariates
- Other transformations (e.g., probit) also have this property
  - but the logit transformation is by far the most widely used in epidemiologic research

Readings

- Chapter 11
  - Hernán MA, Robins JM. *Causal Inference: What If*.

Progress report

1. Introduction to modeling

2. Stratified analysis: Outcome regression