

Biostatistics 208

Lecture 1: Overview & Linear Regression Intro.

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Organization

- Office hours by appointment
(Mission Hall 2540)
- E-mail to make an appointment or get questions answered quickly: stephen.shiboski@ucsf.edu
- Download lecture slides, labs, data & homework from course site:

<https://courses.ucsf.edu/course/view.php?id=2588>

Textbook - VGSM, 2nd edition

Statistics for Biology and Health

Eric Vittinghoff · David Glidden · Steve Shiboski · Charles E. McCulloch

Regression Methods in Biostatistics

Linear, Logistic, Survival, and Repeated Measures Models, *Second Edition*

This new edition provides a unified, in-depth, readable introduction to the multipredictor regression methods most widely used in biostatistics: linear models for continuous outcomes, logistic models for binary outcomes, the Cox model for right-censored survival times, repeated-measures models for longitudinal and hierarchical outcomes, and generalized linear models for counts and other outcomes.

Treating these topics together takes advantage of all they have in common. The authors point out the many-shared elements in the methods they present for selecting, estimating, checking, and interpreting each of these models. They also show that these regression methods deal with confounding, mediation, and interaction of causal effects in essentially the same way.

The examples, analyzed using Stata, are drawn from the biomedical context but generalize to other areas of application. While a first course in statistics is assumed, a chapter reviewing basic statistical methods is included. Some advanced topics are covered but the presentation remains intuitive. A brief introduction to regression analysis of complex surveys and notes for further reading are provided. For many students and researchers learning to use these methods, this one book may be all they need to conduct and interpret multipredictor regression analyses.

In the second edition of *Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models*, the authors have substantially revised and expanded the core chapters of the first edition, and added two new chapters.

From the reviews of the first edition:

"This book provides a unified introduction to the regression methods listed in the title...The methods are well illustrated by data drawn from medical studies... A real strength of this book is the careful discussion of issues common to all of the multipredictor methods covered."
Journal of Biopharmaceutical Statistics, 2005

"This book is not just for biostatisticians. It is, in fact, a very good, and relatively nonmathematical, overview of multipredictor regression models. Although the examples are biologically oriented, they are generally easy to understand and follow...I heartily recommend the book"
Technometrics, February 2006

"Overall, the text provides an overview of regression methods that is particularly strong in its breadth of coverage and emphasis on insight in place of mathematical detail. As intended, this well-unified approach should appeal to students who learn conceptually and verbally."
Journal of the American Statistical Association, March 2006

Statistics / Life Sciences,
Medicine, Health Sciences

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SBH

Vittinghoff · Glidden
Shiboski · McCulloch



Regression Methods in Biostatistics

2nd Ed.

Statistics for Biology and Health

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Regression Methods in Biostatistics

Linear, Logistic, Survival, and Repeated
Measures Models

Second Edition

 Springer

Lectures

- Linear regression for continuous outcomes

7 lectures on simple and multiple linear regression

- Logistic regression for binary outcomes

4 lectures on logistic regression and alternative approaches for binary outcomes

Labs

- Thursdays in Mission Hall 1400
- 10:30-12:00
- Labs show how to use Stata (version14) to apply methods discussed in class
 - Data & commands are included
 - Labs not graded
 - An interpretive handout will be posted after lab
- Labs are a good place to ask questions about advanced topics related to the course, and for help with homework

Homework

- 70% of grade
- Four homework assignments; *missing one can making passing difficult*
- Your responsibility to meet deadlines; late home works not accepted; *if you are going to be out of town, please make arrangements*
- Assignments posted on the course web site (first one will be posted today)
- Completed assignments should be submitted by email (to biostat208hw@gmail.com by 10:30 AM on the due date)
- Handed back the next week with comments and discussion session

Heads up: Biostat 209 Project

This will be a written report of a data analysis, similar to a brief, focused research manuscript but with more statistical detail than usual.

Goal: Address a single substantive issue or a few closely related issues; this should not be a comprehensive report of all findings from a study.

- Students taking 209 next quarter should start thinking about the project now
- Identify a candidate dataset, ideally linked to your own research interests
- The project can be the basis for a submitted abstract/manuscript

Review of Exploratory Data Analysis

- A key part of regression modeling is exploratory data analysis of key variables (as covered in Biostat 200)
- Exploratory assessments should be made prior to any data analysis
- The first assignment & lab review some of these concepts

Review topics (chapter 3 of VGSM)

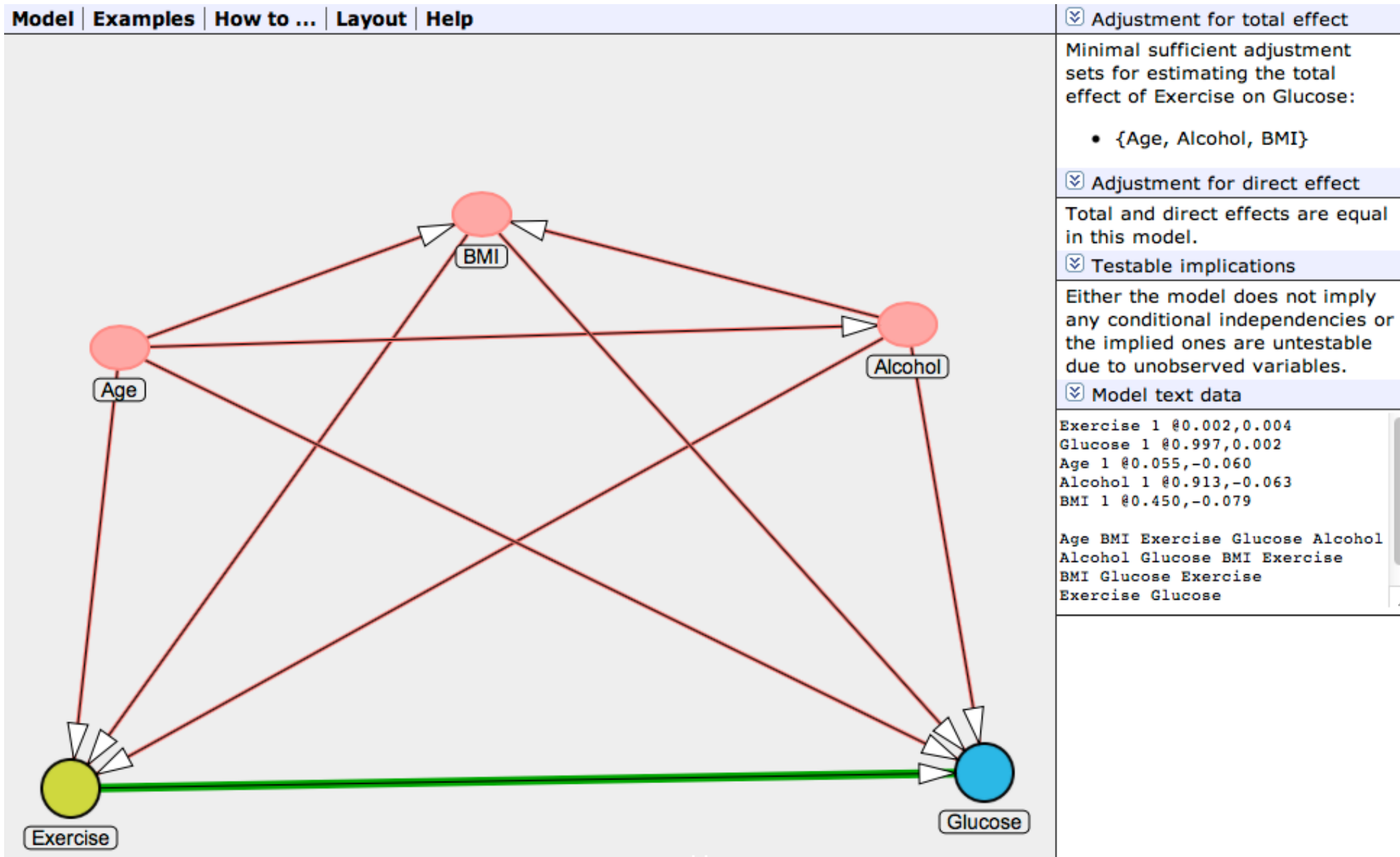
- logarithms & exponentials
- probability distribution; conditional probability; independence
- expectation & conditional expectation
- median, mean, variance, standard deviation, standard error
- correlation coefficient (Pearson & Spearman)
- hypothesis test (1 & 2-sided)
- t-test, ANOVA, chi-squared tests

Regression models for the relationship between outcomes and predictor variables

- Research questions frequently focus on the relationship between an outcome and additional *predictor variables*
- For single categorical predictors (e.g. treatment assignment in randomized trials), simple analysis methods (e.g. *t*-tests & chi squared tests) frequently are enough
- For multiple predictors, and/or continuous predictors (e.g. from observational studies), the relationship with the outcome is frequently very complex
- Statistical models are useful tools for summarizing relationships and making inferences when continuous and/or multiple predictors are involved

Example: relationship between exercise & glucose in HERS (section 4.1 of text)

- Sample DAG (from dagitty.net) suggests adjustment for age, alcohol & BMI



Multiple Predictor Regression Models

- Additive, linear statistical models for the relationship between an outcome and multiple predictor variables (aka “independent”, “risk” or “exposure” variables)
- Outcome types include
 - binary (or categorical) indicators (e.g. *logistic models*)
 - continuous measures (e.g. *linear models*)
 - event times (e.g. *proportional hazards models*)
- Methods can be applied to dependent outcomes (*repeated/clustered*) and a range of study designs (*surveys, case-control*)
- Because regression models make strong assumptions about the relationship between outcome and predictors, assessing validity of assumptions is a critical part of any application

Common Goals in Regression Modeling

- **Evaluating a predictor of primary interest**
 - additional predictors selected both for face validity and on statistical grounds, guided by appropriate DAG(s)
 - focus on confounding, mediation and interaction
 - causal inference
- **Identifying multiple important predictors**
 - variables selected as indicated above
 - addressing issues of confounding, mediation and interaction is complicated; over-fitting & false-positive results become concerns (i.e. control for multiple testing often required)
- **Outcome prediction / risk stratification**
 - focus on minimizing *prediction error*

Contrasting Multiple Regression Approaches

- **Similarities**

- Structural:

- Predictors linked to the some feature of the outcome in an additive, linear fashion:
- *Example*: linear regression
- The conditional mean the outcome (y) is a linear function of the predictors ($x_1, x_2, \dots, x_p$):

$$E[y|x_1, x_2, \dots, x_p] = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p$$

- *Example*: logistic regression
- The conditional odds of outcome occurrence is a log-linear function of the predictors

$$\log\left[\frac{P(x_1, \dots, x_p)}{1 - P(x_1, \dots, x_p)}\right] = \beta_0 + \beta_1 x_1 + \dots + \beta_p x_p$$

Contrasting Multiple Regression Approaches

- **Similarities**

- Operational (methods for using regression in practice are similar for different outcome types)
 - model construction & selection
 - statistical inference
 - model evaluation & assessment

Contrasting Multiple Regression Approaches

- **Differences**

- Differing outcome types require different distributional assumptions
- Interpretation of coefficients and predicted quantities differ between approaches
- Alternative techniques for estimation are involved

Review: linear regression with a single predictor

- Linear model for the relationship between a continuous outcome and categorical/continuous predictor variable

Example: The HERS Study

- **Heart and Estrogen/Progestin Replacement Study**
- Randomized trial of Estrogen + Progestin for secondary prevention of coronary heart disease (CHD) events in postmenopausal women with existing CHD (Hulley S, et al; *JAMA* , 1998)
- 2763 women, ages 46 - 79, followed for an average 4.1 years
- Examples for today based on a random sample of 221 women at study entry
- Focus on the dependence of HDL cholesterol on smoking and waist circumference

Data description from Stata:

```
. describe
```

Contains data from ~/Documents/teaching/c2012/atcr/lecture2/data/hers-sample.dta

```
obs:      221
vars:      3                      18 Jan 2005 08:36
size:     2,431 (99.9% of memory free)
```

variable name	storage type	display format	value label	variable label
smoking	byte	%9.0g	noyes	current smoker
waist	float	%9.0g		waist circumference (cm)
hdl	int	%9.0g		hdl cholesterol (mg/dl)

Sorted by:

Data listing

```
. list hdl smoking waist
```

	hdl	smoking	waist
1.	62	no	85.3
2.	46	no	106.7
3.	29	no	95
4.	52	no	98.2
5.	49	yes	100.7
6.	43	no	88.8
7.	63	yes	88
8.	45	no	102
9.	40	no	85.6
10.	53	no	71.6
11.	49	no	86.6
12.	72	no	74.3
13.	58	no	86
14.	51	no	109.5
15.	57	no	85.1
16.	52	no	139
17.	36	no	84
18.	43	no	119
19.	36	no	94.5
20.	53	yes	104
21.	54	no	76.7
22.	40	no	76.5

```
--more--
```

Listing more info about variables and their characteristics

. codebook

smoking current smoker

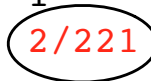
type: numeric (byte)
label: noyes
range: [0,1] units: 1
unique values: 2 missing .: 0/221
tabulation: Freq. Numeric Label
 194 0 no
 27 1 yes

waist waist circumference (cm)

type: numeric (float)
range: [57.5,139] units: .1
unique values: 145 missing .: 0/221
mean: 92.5652
std. dev: 14.5148
percentiles: 10% 25% 50% 75% 90%
 74 82 92.2 102 110

hdl hdl cholesterol (mg/dl)

type: numeric (int)
range: [24,112] units: 1
unique values: 56 missing .: 2/221
mean: 50.2785
std. dev: 13.8306
percentiles: 10% 25% 50% 75% 90%
 36 41 48 57 68



Two indiv. missing HDL

Summaries of included variables

```
. summarize hdl
```

Variable	Obs	Mean	Std. Dev.	Min	Max
hdl	219	50.27854	13.83056	24	112

```
. summarize waist
```

Variable	Obs	Mean	Std. Dev.	Min	Max
waist	221	92.56516	14.51481	57.5	139

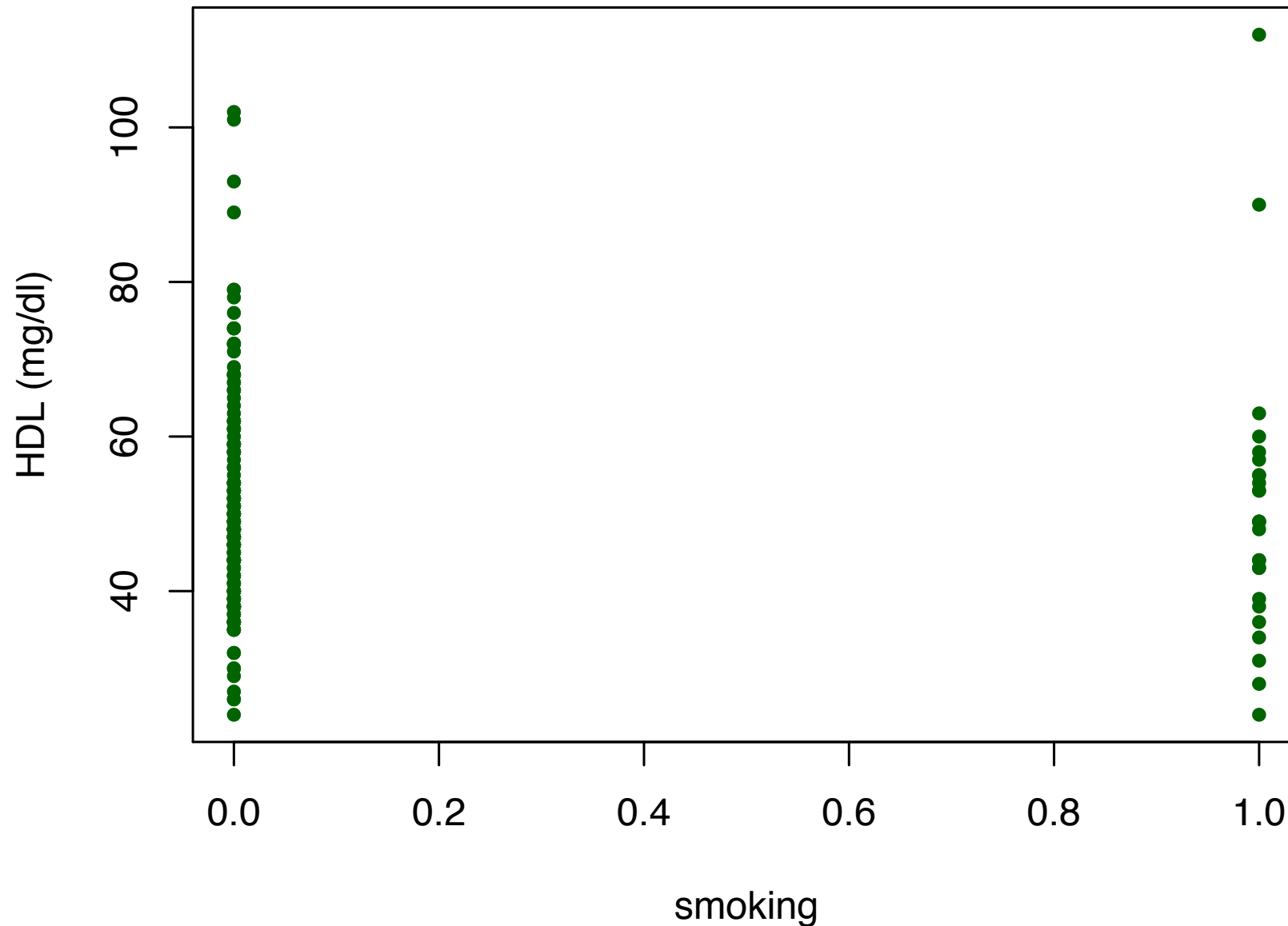
```
. tab smoking
```

current smoker	Freq.	Percent	Cum.
no	194	87.78	87.78
yes	27	12.22	100.00
Total	221	100.00	

Example analyses using HERS data:

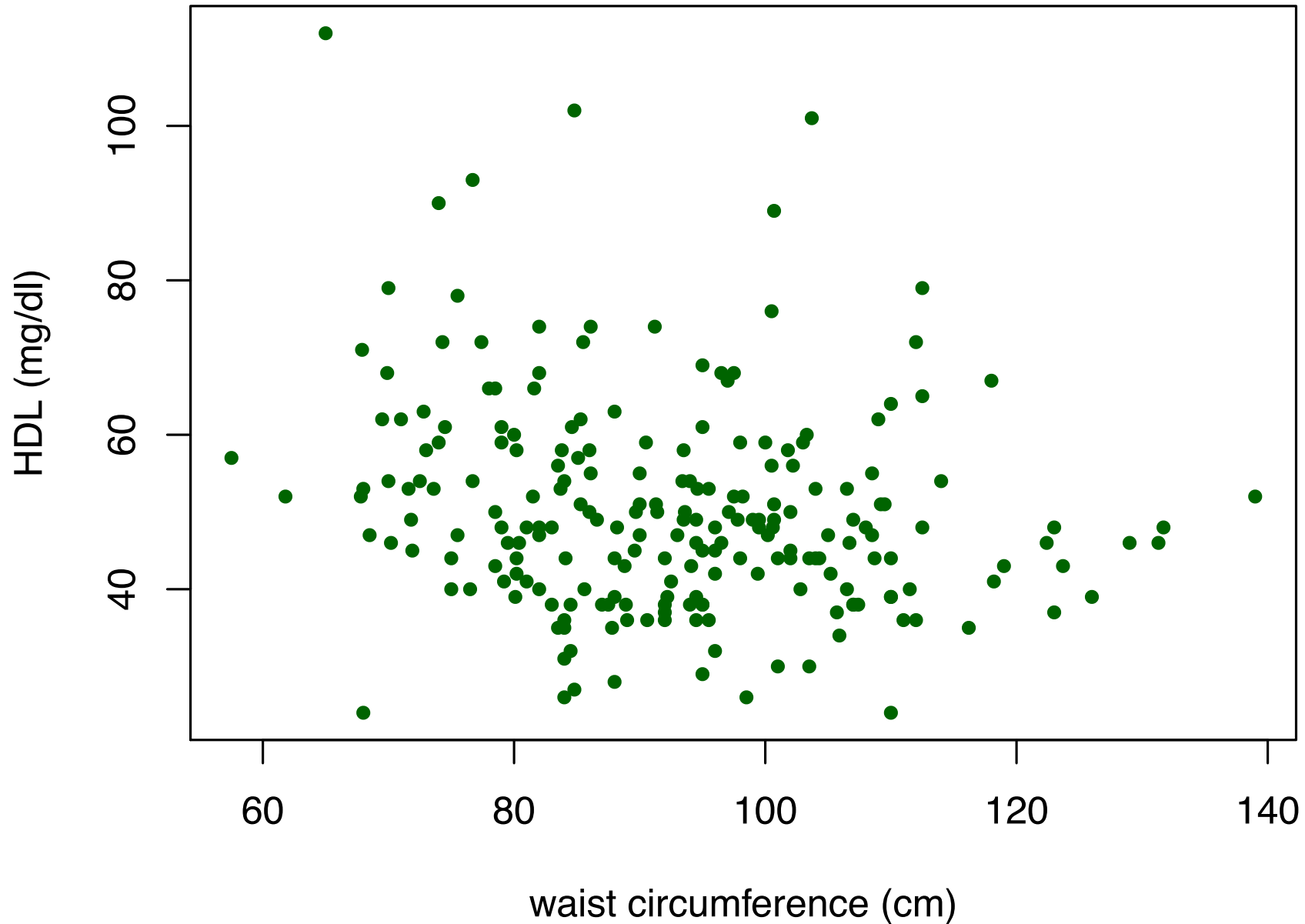
- Relationship between HDL cholesterol (*mg/dl*) and a single binary predictor representing smoking status (*Yes/No*)
- Relationship between HDL cholesterol and a continuous measure of waist circumference (*cm*)

Scatter plot of smoking vs. HDL



Stata command: `twoway (scatter hdl smoking)`

Scatter plot of waist circumference vs. HDL



Stata command: `twoway (scatter hdl waist)`

Linear regression

- Mean of outcome assumed to change linearly with a continuous predictor
- Uses all the data to estimate mean at any point; *borrow strength across points by assuming smoothness*
- Predictor can be of any type: *binary, categorical, count, or continuous*
- Distributional assumptions *not* required for predictor(s)
- Failure of linearity assumption can be addressed via transformations

Systematic part of linear model

- Model represents the *conditional mean* of y as a function of x

$$E[y|x] = \beta_0 + \beta_1 x$$

- Values of $E[y|x]$ lie along the regression line
 - estimated values are known as the *fitted values*

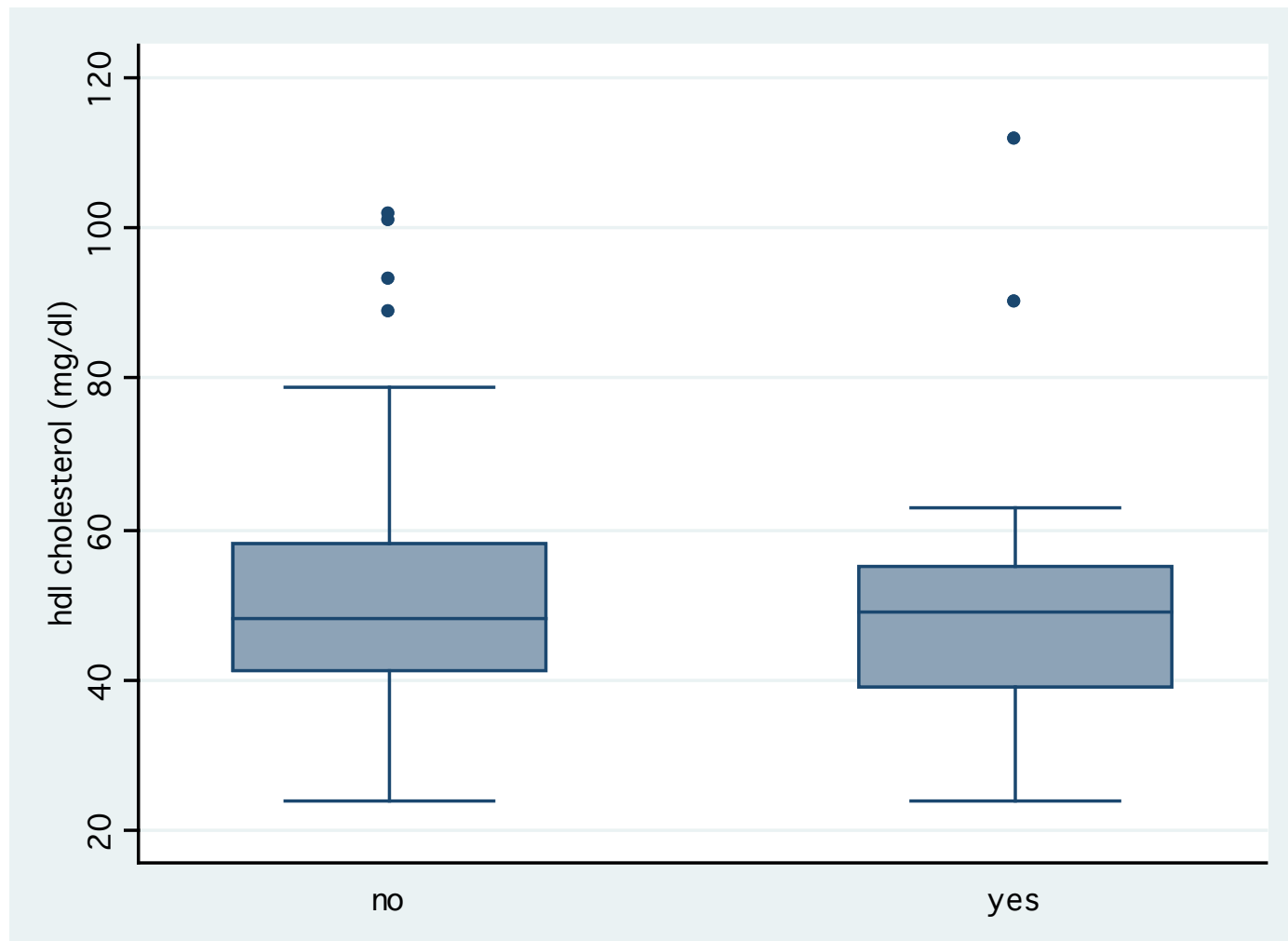
$$\hat{y} = \hat{\beta}_0 + \hat{\beta}_1 x$$

- Dependence on predictor summarized by the slope of the line, β_1
 - β_1 measures change in outcome for a unit increase in x
- Intercept β_0 gives mean of y when $x = 0$

Random part of linear model

- $y = \beta_0 + \beta_1 x + \varepsilon$
 - observed outcome = conditional mean + random error (ε)
 - estimated values of ε are known as *residuals*
- Assumptions about random errors (ε)
 - independent
 - mean zero at all values of x
 - equal variance at all values of x
 - normally distributed (at least in small samples)
- These assumptions are required for valid inference (i.e. for p -values & confidence intervals)
- No assumptions about the predictor are required

HDL by smoking status



Stata command: `graph box hdl, over(smoking)`
(A more informative summary than the scatter plot on slide 23)

A formal comparison of the mean HDL levels between smoking groups can be made using the two-sample *t*-test:

```
. ttest hdl, by(smoking)
```

Two-sample t test with equal variances

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf. Interval]	
no	193	50.26943	.9490756	13.18498	48.39748	52.14138
yes	26	50.34615	3.578114	18.24487	42.97689	57.71542
combined	219	50.27854	.9345828	13.83056	48.43656	52.12051
diff		-.0767238	2.895971		-5.784556	5.631109

diff = mean(no) - mean(yes)

t = -0.0265

Ho: diff = 0

degrees of freedom = 217

Ha: diff < 0

Pr(T < t) = 0.4894

Ha: diff != 0

Pr(|T| > |t|) = 0.9789

Ha: diff > 0

Pr(T > t) = 0.5106

- Regression isn't needed for simple two-group comparisons of means
- A regression model for the above comparison yields identical results:

An simple linear regression model addressing the same hypothesis as the *t*-test from the HDL - smoking example:

```
. regress hdl i.smoking
```

Source	SS	df	MS	Number of obs = 219		
Model	.13487973	1	.13487973	F(1, 217)	=	0.00
Residual	41699.8743	217	192.165319	Prob > F	=	0.9789
Total	41700.0091	218	191.284446	R-squared	=	0.0000
				Adj R-squared	=	-0.0046
				Root MSE	=	13.862

hdl	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
1.smoking	.0767238	2.895971	0.03	0.979	-5.631109	5.784556
_cons	50.26943	.9978353	50.38	0.000	48.30274	52.23612

- Regression output provides the estimated diff. between groups, mean HDL in non-smoking group, but not mean HDL in smoking group. (Means for all groups can be obtained via *postestimation* commands in Stata.)
- Inference about the effect of smoking identical to the previous analysis

Interpretation of linear regression model for single binary predictor (smoking status):

<i>Group</i>	<i>Mean HDL</i>
--------------	-----------------

Overall: $E[y | x] = \beta_0 + \beta_1 x$

smokers ($x = 1$): $\beta_0 + \beta_1$

non-smokers ($x = 0$): β_0

Interpretation of β_1 : Difference in mean HDL between smokers and non-smokers

Note on categorical predictors in regression models:

- Binary predictors coded as 0/1 can be entered directly in regression models without concerns about coding
- A linear regression model with a single binary predictor gives results equivalent to a two-sample *t*-test comparing the means in the groups specified by the predictor
- Categorical variables with >2 levels can be entered in a regression model via binary indicators for each level, reserving one as the reference category
- A linear regression for a single categorical variable with >2 levels is equivalent to a one-way analysis of variance

Post-estimation commands in Stata

- After a regression model is fitted via `regress`, Stata saves a number of values related to the fit that can be used for *post-estimation* analyses. These include:
 - Regression coefficients
 - Standard errors and model statistics
- Common post-estimation analyses include
 - use of `predict` command to compute:
 - *fitted values*
 - *residuals*
 - *influence statistics*
 - use of `lincom` command to estimate means in specific subgroups defined by the model

Post-estimation commands in Stata

Example: using `predict` to estimate fitted values and residuals.

```
. predict yfit, xb  
  
. predict yres, residuals  
  
. list yfit yres hdl smoking if _n<=10
```

	yfit	yres	hdl	smoking
1.	50.26943	11.73057	62	no
2.	50.26943	-4.26943	46	no
3.	50.26943	-21.26943	29	no
4.	50.26943	1.73057	52	no
5.	50.34615	-1.346154	49	yes
6.	50.26943	-7.26943	43	no
7.	50.34615	12.65385	63	yes
8.	50.26943	-5.26943	45	no
9.	50.26943	-10.26943	40	no
10.	50.26943	2.73057	53	no

Note : model only yields two unique fitted values since `smoking` takes on only two values

Post-estimation commands in Stata

Example: using `lincom` to estimate the mean outcome value for smokers and non-smokers in the previous example (recall slide 29).

Issued immediately after a `regress` command, `lincom` provides estimates of **linear combinations** of the estimated regression coefficients, and also provides a std. error and confidence interval:

```
. lincom _cons + smoking
```

smoking	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
(1)	50.34615	2.718635	18.52	0.000	44.98784	55.70446

```
. lincom _cons
```

hdl	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
(1)	50.26943	.9978353	50.38	0.000	48.30274	52.23612

Note : the second command returns the intercept

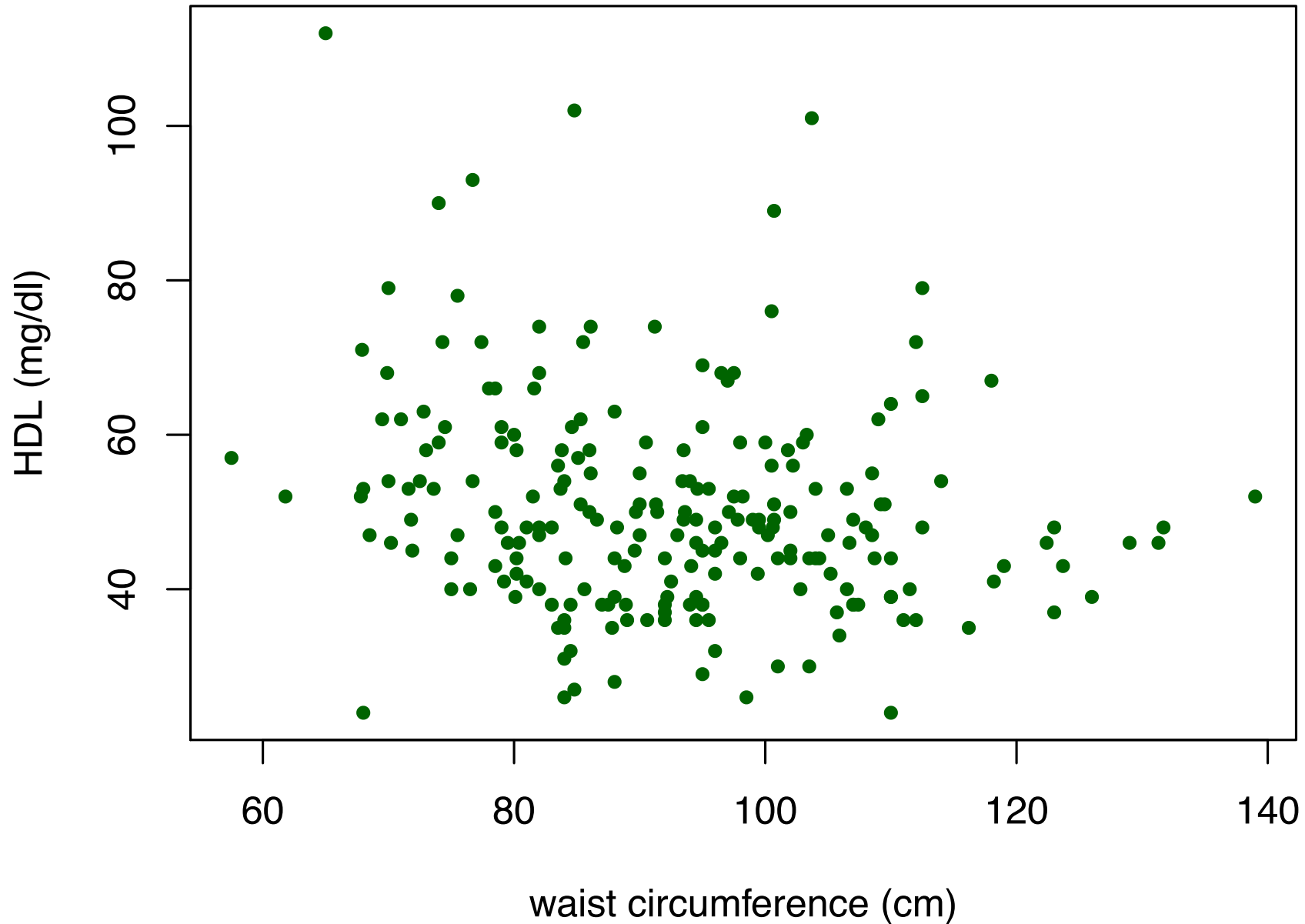
Simple linear regression with a continuous predictor

- A tool for understanding dependence of the mean of a continuous outcome on a single continuous predictor
- With a continuous predictor, summary of dependence is a “line of means”

Example analysis topic:

Relationship between HDL (mg/dl) and the continuous measure waist circumference (cm)

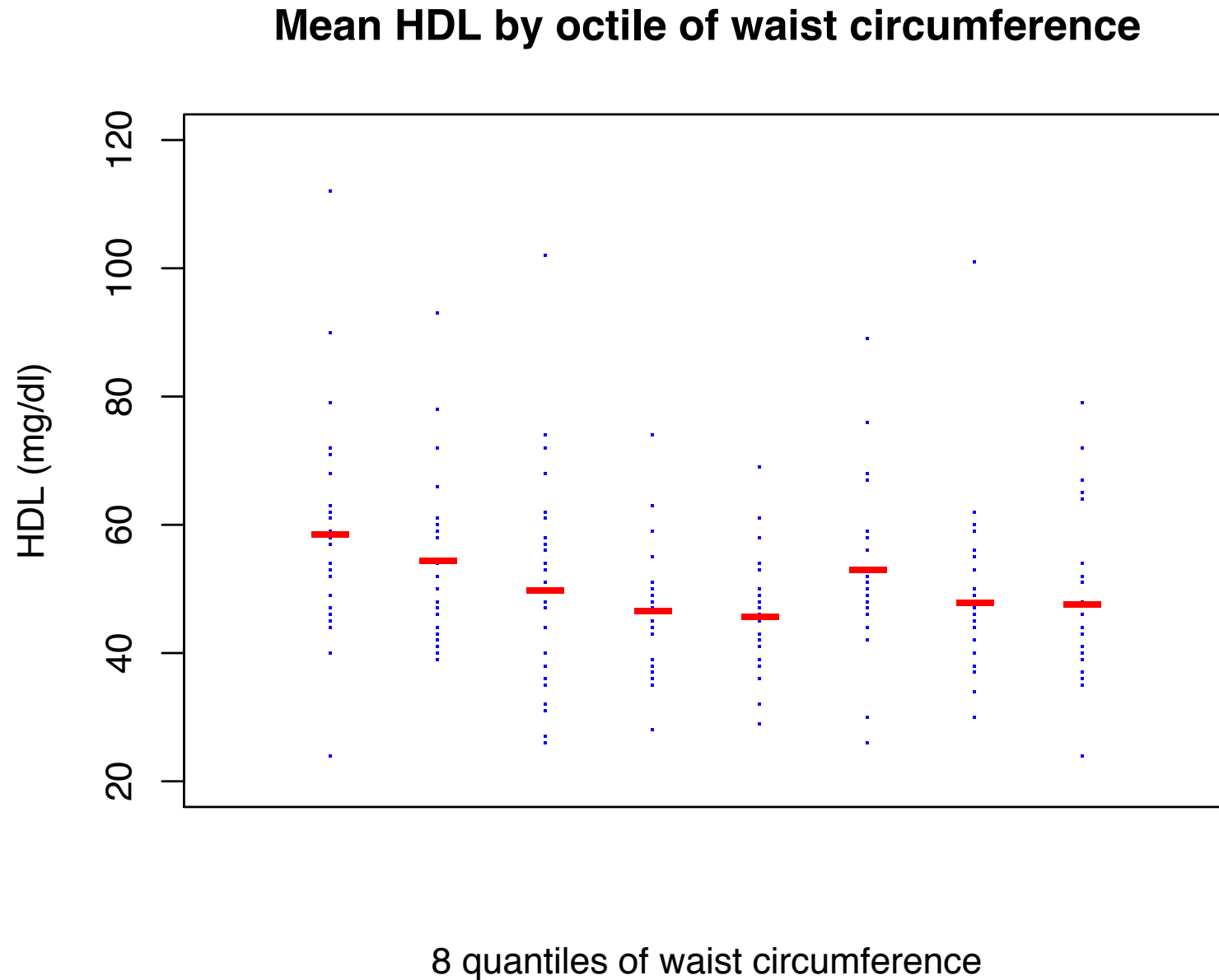
Scatter plot of waist circumference vs. HDL



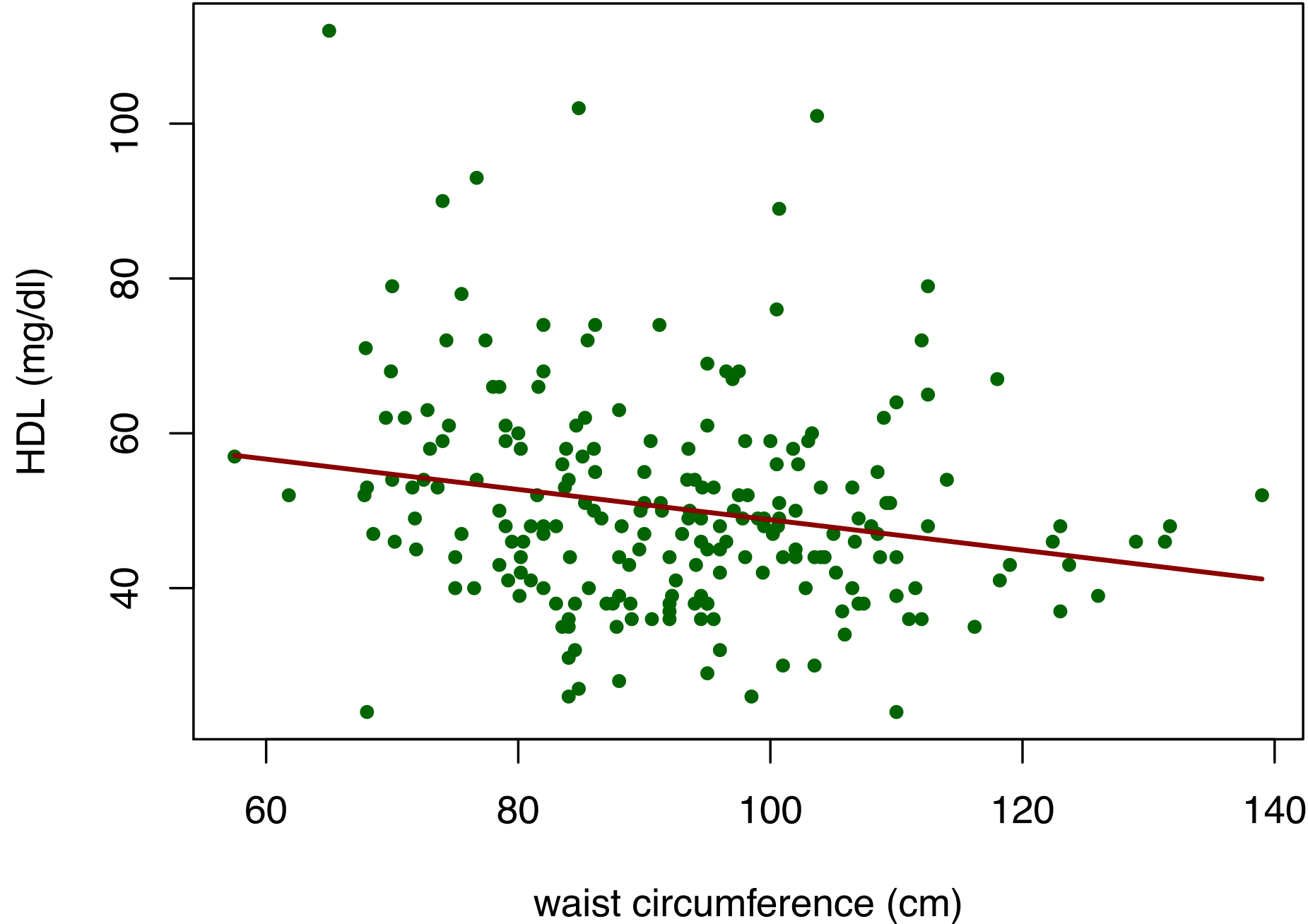
Stata command: `twoway (scatter hdl waist)`

Visualization of relationship without assuming a model:

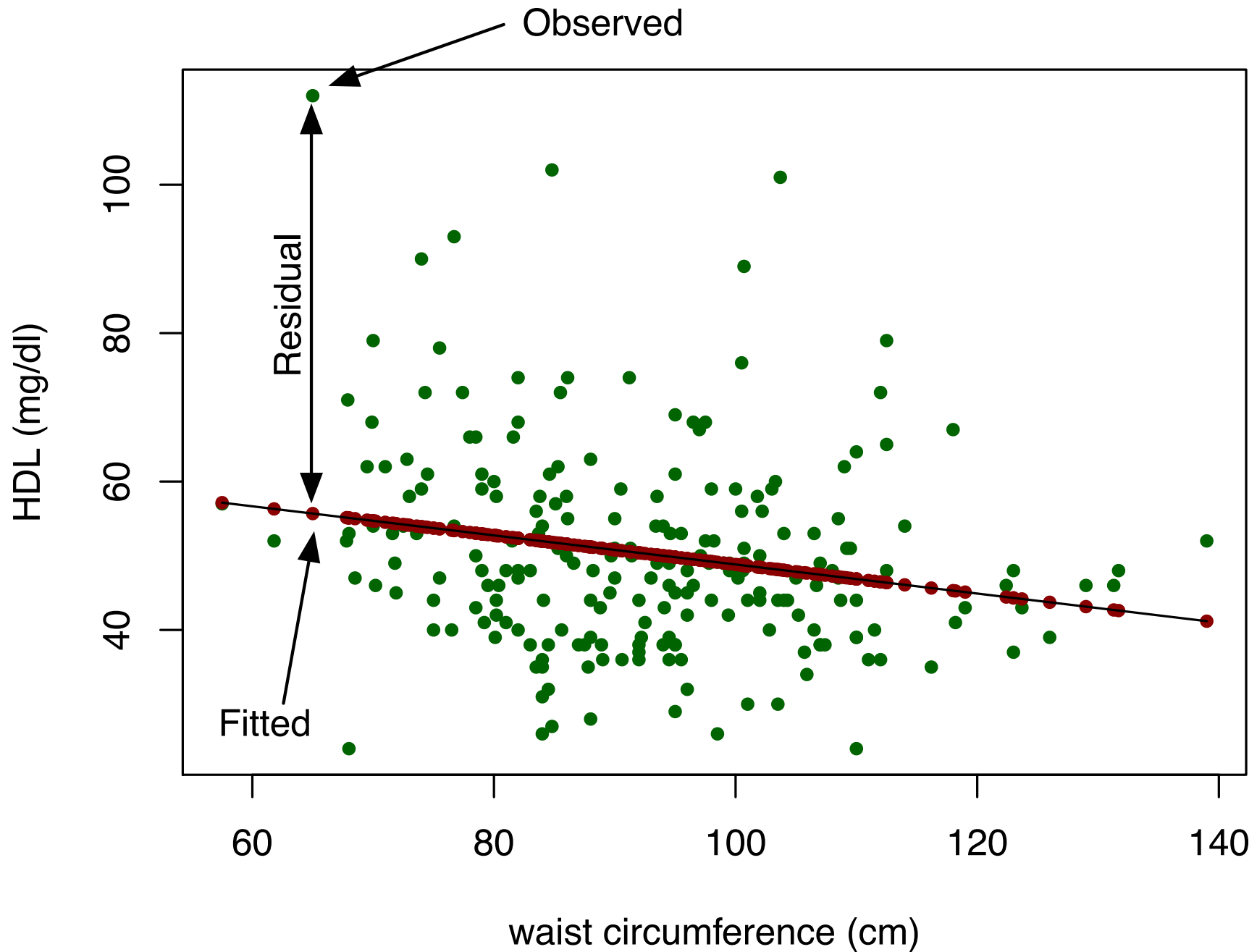
- plotting means in groups defined by quantiles of waist



Linear regression model: mean HDL is linearly related to waist circumference



Observed data, fitted value, residual



Ordinary least squares (OLS) estimation

- Slope and intercept estimated using OLS
- OLS estimates
 - *determine the regression line*
 - *minimize sum of squared residuals (RSS)*

$$\text{TSS} = \sum_{i=1}^n (y_i - \bar{y})^2 \quad \text{MSS} = \sum_{i=1}^n (\hat{y}_i - \bar{y})^2 \quad \text{RSS} = \sum_{i=1}^n (y_i - \hat{y}_i)^2$$

- $\text{TSS} = \text{MSS} + \text{RSS}$ (total SS = model SS + resid. SS)
- Efficient - *minimum variance in class of estimators*
- Maximum likelihood estimates (MLEs) if outcome is normal
- Drawback of OLS: sensitive to outliers

Dependence of HDL on waist circumference

. regress hdl waist

Source	SS	df	MS	Number of obs = 219		
Model	1777.68854	1	1777.68854	F(1, 217) = 9.66		
Residual	39922.3206	217	183.973828	Prob > F = 0.0021		
Total	41700.0091	218	191.284446	R-squared = 0.0426		
				Adj R-squared = 0.0382		
				Root MSE = 13.564		

hdl	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
waist	-.1960017	.0630536	-3.11	0.002	-.3202776	-.0717258
_cons	68.42785	5.910124	11.58	0.000	56.77925	80.07644

The sample estimate of β_1 gives estimated change in mean HDL for each unit increase in waist circ. (in cm)

Mean HDL decreases by about -0.2 mg/dL for each centimeter increase in waist circumference

Precision and statistical significance of slope estimate

```
. regress hdl waist
```

Source	SS	df	MS	Number of obs = 219		
Model	1777.68854	1	1777.68854	F(1, 217) = 9.66		
Residual	39922.3206	217	183.973828	Prob > F = 0.0021		
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hdl	Coef.	Std. Err.	t	P> t 	[95% Conf. Interval]	
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_cons	68.42785	5.910124	11.58	0.000	56.77925	80.07644

The standard error of the estimate for β_1

Model t -statistics are calculated as the ratio $\text{coeff.} / \text{std. error}$. The associated hypothesis tests evaluate the null hypoth. that the true value of the coefficients are zero.

The F statistic evaluates the significance of the improvement in the model including the predictor relative to one that excludes the predictor (i.e. that only estimates the overall mean HDL)

Proportion of variation explained

```
. regress hdl waist
```

Source	SS	df	MS	Number of obs	=	219
Model	1777.68854	1	1777.68854	F(1, 217)	=	9.66
Residual	39922.3206	217	183.973828	Prob > F	=	0.0021
Total	41700.0091	218	191.284446	R-squared	=	0.0426
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waist	-.1960017	.0630536	-3.11	0.002	-.3202776	-.0717258
_cons	68.42785	5.910124	11.58	0.000	56.77925	80.07644

- R-squared is the proportion of total variance in the outcome explained by the regression model:

$$1777.68854/41700.0091 = 0.0426$$

- Adjusted R-squared accounts for the number of predictors in the model

Marginal and residual variance estimates

```
. regress hdl waist
```

Source	SS	df	MS	Number of obs = 219		
Model	1777.68854	1	1777.68854	F(1, 217) = 9.66		
Residual	39922.3206	217	183.973828	Prob > F = 0.0021		
Total	41700.0091	218	191.284446	R-squared = 0.0426		
				Adj R-squared = 0.0382		
				Root MSE = 13.564		

hdl	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
waist	-.1960017	.0630536	-3.11	0.002	-.3202776	-.0717258
_cons	68.42785	5.910124	11.58	0.000	56.77925	80.07644

- The total mean squared error (MS) is the variance of the outcome
- Root mean squared error (MSE) is an index of model accuracy
- The F statistic is the ratio of the model MS to the residual MS
- The t statistic is the square root of the F

Interpreting coefficients from the linear model

- Model represents the mean of HDL as a function of waist circumference
 - $\text{mean}(HDL \mid \text{waist circ.}) = 68.43 - 0.196 \times (\text{waist circ.})$
- 68.43 gives mean HDL for an individual with waist circumference of 0 cm
- -0.196 gives change in aver. HDL assoc. with a 1 cm increase in waist circ.
 - $\text{mean}(HDL \mid \text{waist circ.} = 100) - \text{mean}(HDL \mid \text{waist circ.} = 99) =$
 $[68.43 - 0.196 \times (100)] - [68.43 - 0.196 \times (99)] = -0.196$
- Use model to compute change in aver. HDL assoc. with a 10 unit increase in waist circ.
 - $\text{mean}(HDL \mid \text{waist circ.} = 100) - \text{mean}(HDL \mid \text{waist circ.} = 90) =$
 $[68.43 - 0.196 \times (100)] - [68.43 - 0.196 \times (90)] = -0.196 \times 10$
 $= -1.96$

Regression post-estimation commands

- Issued after fitting a regression model
- Used for model assessment and interpretation

Example: using `lincom` to estimate the mean outcome for an individual with waist size of 120 cm.

```
. lincom _cons + waist*120
```

```
( 1) 120*waist + _cons = 0
```

hd1	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
(1)	44.90764	1.955863	22.96	0.000	41.05272 48.76257

Example: using `lincom` to estimate the change in mean outcome for a 10 cm increase in waist size.

```
. lincom waist*10
```

```
( 1) 10*waist = 0
```

hd1	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
(1)	-1.960017	.6305362	-3.11	0.002	-3.202776 -.7172577

Post-estimation commands

Example: The `predict` command is used to estimate fitted values and residuals.

```
. predict yfit, xb  
. predict yres, residuals  
(2 missing values generated)
```

```
. list if _n<=10
```

	smoking	waist	hdl	yfit	yres
1.	no	85.3	62	51.7089	10.2911
2.	no	106.7	46	47.51447	-1.514468
3.	no	95	29	49.80769	-20.80769
4.	no	98.2	52	49.18048	2.819518
5.	yes	100.7	49	48.69048	.3095219
6.	no	88.8	43	51.0229	-8.022897
7.	yes	88	63	51.1797	11.8203
8.	no	102	45	48.43568	-3.435675
9.	no	85.6	40	51.6501	-11.6501
10.	no	71.6	53	54.39413	-1.394127

Note : model yields unique fitted values for distinct values of smoking and waist

Questions a simple linear regression can answer

1. How does mean of outcome depend on predictor?
2. What is the precision of the estimated association, and is it statistically significant?
3. How much of overall variation in the outcome is explained by the estimated linear model?

Summarizing regression results

“In unadjusted analysis, higher values of waist circumference were associated with lower average levels of HDL (0.2 mg/dL lower HDL per cm increase in waist circumference; 95% CI -0.32 to -0.07, $p = 0.002$). However, waist circumference accounted for only 4% of the variability in HDL.”

A good summary

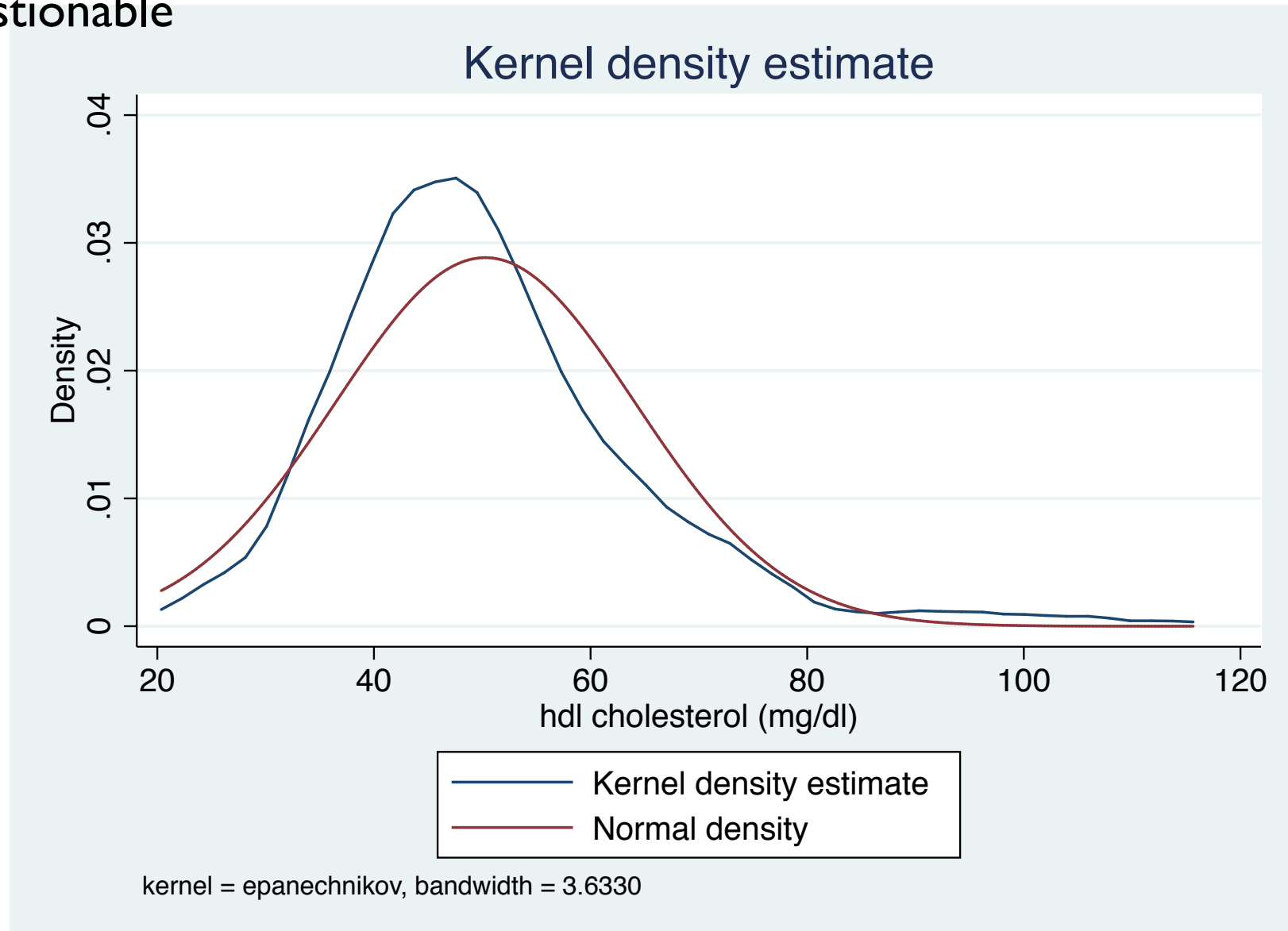
- Doesn't just focus on statistical significance
- Cites slope estimate *and* 95% CI
- Uses sensible “units” for slope
- May use *R*-squared as a measure of substantive importance

Special Topic: Bootstrap confidence intervals

- When assumptions required for statistical inference from regression models are violated, the *bootstrap* can be used to help obtain valid inferences (Section 3.6,VGSM)
- Bootstrapping involves drawing repeated samples with replacement from the original sample, and estimating the quantities of interest from each. The variability in these estimates is used to obtain confidence intervals
- Bootstrap confidence intervals are “nonparametric” in the sense that they avoid distributional assumptions typically required for inferences from regression models
- Typically, a large number of samples (e.g. 1000) is required

Example: Bootstrap confidence interval for HDL - waist circumference model

- Exploratory analysis reveals that normality of the distribution of HDL is questionable



Stata command: `kdensity hdl, normal`

Example: Bootstrap confidence interval for HDL - waist circumference model

```
. bootstrap `regress hdl waist' _b, reps(1000)
```

```
command:      regress hdl waist
statistics:    b_waist      = _b[waist]
               b_cons       = _b[_cons]
```

Bootstrap statistics

Number of obs = 219

Replications = 1000

Variable	Reps	Observed	Bias	Std. Err.	[95% Conf. Interval]		
b_waist	1000	-.1960017	-.0012388	.0667359	-.3269603	-.0650432	(N)
					-.3373865	-.0717307	(P)
					-.3401462	-.0727492	(BC)
b_cons	1000	68.42785	.1313524	6.41104	55.8472	81.0085	(N)
					56.19201	81.75299	(P)
					56.11214	81.73902	(BC)

Note: N = normal
P = percentile
BC = bias-corrected

- In this case, inferences largely unchanged compared to standard approach (see slide #43)