Data Science for Biological, Medical and Health Research: Notes for 432

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Introduction

These Notes provide a series of examples using R to work through issues that are likely to come up in PQHS/CRSP/MPHP 432.

While these Notes share some of the features of a textbook, they are neither comprehensive nor completely original. The main purpose is to give students in 432 a set of common materials on which to draw during the course. In class, we will sometimes:

- reiterate points made in this document,
- amplify what is here,
- simplify the presentation of things done here,
- use new examples to show some of the same techniques,
- refer to issues not mentioned in this document,

but what we don't (always) do is follow these notes very precisely. We assume instead that you will read the materials and try to learn from them, just as you will attend classes and try to learn from them. We welcome feedback of all kinds on this document or anything else. Just email us at 431-help at case dot edu, or submit a pull request. Note that we still use 431-help even though we're now in 432.

What you will mostly find are brief explanations of a key idea or summary, accompanied (most of the time) by R code and a demonstration of the results of applying that code.

Everything you see here is available to you as HTML or PDF. You will also have access to the R Markdown files, which contain the code which generates everything in the document, including all of the R results. We will demonstrate the use of R Markdown (this document is generated with the additional help of an R package called bookdown) and R Studio (the "program" which we use to interface with the R language) in class.

To download the data and R code related to these notes, visit the Data and Code section of the 432 course website.

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R Packages used in these notes

Here, we'll load in the packages used in these notes.

```
library(tableone)
library(skimr)
library(broom)
library(magrittr)
library(modelr)
library(tidyverse)
```

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Data used in these notes

Here, we'll load in the data sets used in these notes.

```
fakestroke <- read.csv("data/fakestroke.csv") %>% tbl_df
bloodbrain <- read.csv("data/bloodbrain.csv") %>% tbl_df
smartcle1 <- read.csv("data/smartcle1.csv") %>% tbl_df
```

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Chapter 1

Building Table 1

Many scientific articles involve direct comparison of results from various exposures, perhaps treatments. In 431, we studied numerous methods, including various sorts of hypothesis tests, confidence intervals, and descriptive summaries, which can help us to understand and compare outcomes in such a setting. One common approach is to present what's often called Table 1. Table 1 provides a summary of the characteristics of a sample, or of groups of samples, which is most commonly used to help understand the nature of the data being compared.

1.1 Two examples from the New England Journal of Medicine

1.1.1 A simple Table 1

Table 1 is especially common in the context of clinical research. Consider the excerpt below, from a January 2015 article in the New England Journal of Medicine (Tolaney et al., 2015).

Table 1. Baseline Characteristics of the Patients.*								
Characteristic	Patients (N=406)							
	no. (%)							
Age group								
<50 yr	132 (32.5)							
50–59 yr	137 (33.7)							
60–69 yr	96 (23.6)							
≥70 yr	41 (10.1)							
Sex								
Female	405 (99.8)							
Male	1 (0.2)							
Race†								
White	351 (86.5)							
Black	28 (6.9)							
Asian	11 (2.7)							
Other	16 (3.9)							

This (partial) table reports baseline characteristics on age group, sex and race, describing 406 patients with

HER2-positive¹ invasive breast cancer that began the protocol therapy. Age, sex and race (along with severity of illness) are the most commonly identified characteristics in a Table 1.

In addition to the measures shown in this excerpt, the full Table also includes detailed information on the primary tumor for each patient, including its size, nodal status and histologic grade. Footnotes tell us that the percentages shown are subject to rounding, and may not total 100, and that the race information was self-reported.

1.1.2 A group comparison

A more typical Table 1 involves a group comparison, for example in this excerpt from Roy et al. (2008). This Table 1 describes a multi-center randomized clinical trial comparing two different approaches to caring for patients with heart failure and atrial fibrillation².

Table 1. Baseline Characteristics of the Patients.*		
Variable	Rhythm-Control Group (N = 682)	Rate-Control Group (N = 694)
Male sex (%)	78	85
Age (yr)	66±11	67±11
Body-mass index†	27.8±5.4	28.0±5.1
Nonwhite race (%)‡	16	13
NYHA class III or IV (%)		
At baseline	32	31
During previous 6 mo	76	76
Predominant cardiac diagnosis (%)∫		
Coronary artery disease	48	48
Valvular heart disease	5	5
Nonischemic cardiomyopathy	36	39
Congenital heart disease	1	1
Hypertensive heart disease	10	7

The article provides percentages, means and standard deviations across groups, but note that it does not provide p values for the comparison of baseline characteristics. This is a common feature of NEJM reports on randomized clinical trials, where we anticipate that the two groups will be well matched at baseline. Note that the patients in this study were *randomly* assigned to either the rhythm-control group or to the rate-control group, using blocked randomizations stratified by study center.

1.2 The MR CLEAN trial

Berkhemer et al. (2015) reported on the MR CLEAN trial, involving 500 patients with acute ischemic stroke caused by a proximal intracranial arterial occlusion. The trial was conducted at 16 medical centers in the Netherlands, where 233 were randomly assigned to the intervention (intraarterial treatment plus usual care) and 267 to control (usual care alone.) The primary outcome was the modified Rankin scale score at 90 days; this categorical scale measures functional outcome, with scores ranging from 0 (no symptoms) to 6 (death). The fundamental conclusion of Berkhemer et al. (2015) was that in patients with acute ischemic stroke

¹HER2 = human epidermal growth factor receptor type 2. Over-expression of this occurs in 15-20% of invasive breast cancers, and has been associated with poor outcomes.

²The complete Table 1 appears on pages 2668-2669 of Roy et al. (2008), but I have only reproduced the first page and the footnote in this excerpt.

caused by a proximal intracranial occlusion of the anterior circulation, intraarterial treatment administered within 6 hours after stroke onset was effective and safe.

Here's the Table 1 from Berkhemer et al. (2015).

Characteristic	Intervention (N = 233)	Control (N = 267)
Age — yr		
Median	65.8	65.7
Interquartile range	54.5-76.0	55.5-76.4
Male sex — no. (%)	135 (57.9)	157 (58.8)
NIHSS score†		
Median (interquartile range)	17 (14–21)	18 (14-22)
Range	3-30	4-38
Location of stroke in left hemisphere — no. (%)	116 (49.8)	153 (57.3)
History of ischemic stroke — no. (%)	29 (12.4)	25 (9.4)
Atrial fibrillation — no. (%)	66 (28.3)	69 (25.8)
Diabetes mellitus — no. (%)	34 (14.6)	34 (12.7)
Prestroke modified Rankin scale score — no. (%)‡		
0	190 (81.5)	214 (80.1)
1	21 (9.0)	29 (10.9)
2	12 (5.2)	13 (4.9)
>2	10 (4.3)	11 (4.1)
Systolic blood pressure — mm Hg∫	146±26.0	145±24.4
Treatment with IV alteplase — no. (%)	203 (87.1)	242 (90.6)
Time from stroke onset to start of IV alteplase — min		
Median	85	87
Interquartile range	67-110	65-116
ASPECTS — median (interquartile range)¶	9 (7-10)	9 (8-10)
Intracranial arterial occlusion — no./total no. (%)		
Intracranial ICA	1/233 (0.4)	3/266 (1.1)
ICA with involvement of the M1 middle cerebral artery segment	59/233 (25.3)	75/266 (28.2)
M1 middle cerebral artery segment	154/233 (66.1)	165/266 (62.0)
M2 middle cerebral artery segment	18/233 (7.7)	21/266 (7.9)
A1 or A2 anterior cerebral artery segment	1/233 (0.4)	2/266 (0.8)
Extracranial ICA occlusion — no./total no. (%) **	75/233 (32.2)	70/266 (26.3)
Time from stroke onset to randomization — min††		
Median	204	196
Interquartile range	152-251	149–266
Time from stroke onset to groin puncture — min		
Median	260	NA
Interquartile range	210-313	

The Table was accompanied by the following notes.

- * The intervention group was assigned to intraarterial treatment plus usual care, and the control group was assigned to usual care alone. Plus-minus values are means ±SD. ICA denotes internal carotid artery, IV intravenous, and NA not applicable.
- † Scores on the National Institutes of Health Stroke Scale (NIHSS) range from 0 to 42, with higher scores indicating more severe neurologic deficits. The NIHSS is a 15-item scale, and values for 30 of the 7500 items were missing (0.4%). The highest number of missing items for a single patient was 6.
- Scores on the modified Rankin scale of functional disability range from 0 (no symptoms) to 6 (death). A score of 2 or less indicates functional independence.
- Data on systolic blood pressure at baseline were missing for one patient assigned to the control group.
- The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) is a measure of the extent of stroke. Scores ranges from 0 to 10, with higher scores indicating fewer early ischemic changes. Scores were not available for four patients assigned to the control group: noncontrast computed tomography was not performed in one patient, and three patients had strokes in the territory of the anterior cerebral artery.
- Vessel imaging was not performed in one patient in the control group, so the level of occlusion was not known.
- ** Extracranial ICA occlusions were reported by local investigators.
- †† Data were missing for two patients in the intervention group.

1.3 Simulated fakestroke data

Consider the simulated data, available on the Data and Code page of our course website in the fakestroke.csv file, which I built to let us mirror the Table 1 for MR CLEAN (Berkhemer et al., 2015). The fakestroke.csv file contains the following 18 variables for 500 patients.

studyid	Study ID # (z001 through z500)
trt	Treatment group (Intervention or Control)
age	Age in years
sex	Male or Female
nihss	NIH Stroke Scale Score (can range from 0-42; higher scores
	indicate more severe neurological deficits)
location	Stroke Location - Left or Right Hemisphere
hx.isch	History of Ischemic Stroke (Yes/No)
afib	Atrial Fibrillation $(1 = Yes, 0 = No)$
dm	Diabetes Mellitus $(1 = Yes, 0 = No)$
mrankin	Pre-stroke modified Rankin scale score $(0, 1, 2 \text{ or } > 2)$
	indicating functional disability - complete range is 0 (no
	symptoms) to 6 (death)
sbp	Systolic blood pressure, in mm Hg
iv.altep	Treatment with IV alterplase (Yes/No)
time.iv	Time from stroke onset to start of IV alteplase (minutes) if
	iv.altep=Yes
aspects	Alberta Stroke Program Early Computed Tomography
	score, which measures extent of stroke from 0 - 10; higher
	scores indicate fewer early ischemic changes
ia.occlus	Intracranial arterial occlusion, based on vessel imaging -
	five categories ³
extra.ica	Extracranial ICA occlusion $(1 = Yes, 0 = No)$
time.rand	Time from stroke onset to study randomization, in minutes
time.punc	Time from stroke onset to groin puncture, in minutes (only
	if Intervention)

Here's a quick look at the simulated data in fakestroke.

³The five categories are Intracranial ICA, ICA with involvement of the M1 middle cerebral artery segment, M1 middle cerebral artery segment, M2 middle cerebral artery segment, A1 or A2 anterior cerebral artery segment

fakestroke

```
# A tibble: 500 x 18
   studyid trt
                      age sex
                                nihss location hx.isch afib
                                                                 dm mrankin
           <fct>
   <fct>
                    <dbl> <fct> <int> <fct>
                                                <fct>
                                                        <int> <int> <fct>
 1 z001
           Control 53.0 Male
                                                            0
                                                                  0 2
                                   21 Right
                                                No
 2 z002
           Interve~ 51.0 Male
                                                                  0 0
                                   23 Left
                                                No
                                                            1
                     68.0 Fema~
 3 z003
                                                            0
                                                                  0 0
           Control
                                   11 Right
                                                No
 4 z004
           Control
                     28.0 Male
                                   22 Left
                                                No
                                                            0
                                                                  0 0
                                                            0
 5 z005
           Control
                     91.0 Male
                                   24 Right
                                                No
                                                                  0 0
 6 z006
           Control
                     34.0 Fema~
                                   18 Left
                                                No
                                                                  0 2
 7 z007
                                   25 Right
                                                            0
                                                                  0 0
           Interve~ 75.0 Male
                                                No
 8 z008
           Control
                     89.0 Fema~
                                   18 Right
                                                No
                                                            0
                                                                  0 0
9 z009
           Control
                     75.0 Male
                                   25 Left
                                                No
                                                            1
                                                                  0 2
10 z010
           Interve~ 26.0 Fema~
                                   27 Right
                                                            0
                                                                  0 0
                                                No
# ... with 490 more rows, and 8 more variables: sbp <int>, iv.altep <fct>,
   time.iv <int>, aspects <int>, ia.occlus <fct>, extra.ica <int>,
   time.rand <int>, time.punc <int>
```

1.4 Building Table 1 for fakestroke: Attempt 1

Our goal, then, is to take the data in fakestroke.csv and use it to generate a Table 1 for the study that compares the 233 patients in the Intervention group to the 267 patients in the Control group, on all of the other variables (except study ID #) available. I'll use the tableone package of functions available in R to help me complete this task. We'll make a first attempt, using the CreateTableOne function in the tableone package. To use the function, we'll need to specify:

- the vars or variables we want to place in the rows of our Table 1 (which will include just about everything in the fakestroke data except the studyid code and the trt variable for which we have other plans, and the time.punc which applies only to subjects in the Intervention group.)
 - A useful trick here is to use the dput function, specifically something like dput (names (fakestroke)) can be used to generate a list of all of the variables included in the fakestroke tibble, and then this can be copied and pasted into the vars specification, saving some typing.
- the strata which indicates the levels want to use in the columns of our Table 1 (for us, that's trt)

Stratified by trt Control Intervention test 267 233 age (mean (sd)) 65.38 (16.10) 63.93 (18.09) 0.343 sex = Male (%) 157 (58.8) 135 (57.9) 0.917 nihss (mean (sd)) 18.08 (4.32) 17.97 (5.04) 0.787 117 (50.2) location = Right (%) 114 (42.7) 0.111

hx.isch = Yes (%)	25	(9.4)	29	(12.4)	0.335
afib (mean (sd))	0.26	(0.44)	0.28	(0.45)	0.534
dm (mean (sd))	0.13	(0.33)	0.12	(0.33)	0.923
mrankin (%)					0.922
> 2	11	(4.1)	10	(4.3)	
0	214	(80.1)	190	(81.5)	
1	29	(10.9)	21	(9.0)	
2	13	(4.9)	12	(5.2)	
sbp (mean (sd))	145.00	(24.40)	146.03	(26.00)	0.647
iv.altep = Yes (%)	242	(90.6)	203	(87.1)	0.267
time.iv (mean (sd))	87.96	(26.01)	98.22	(45.48)	0.003
aspects (mean (sd))	8.65	(1.47)	8.35	(1.64)	0.033
ia.occlus (%)					0.795
A1 or A2	2	(0.8)	1	(0.4)	
ICA with M1	75	(28.2)	59	(25.3)	
Intracranial ICA	3	(1.1)	1	(0.4)	
M1	165	(62.0)	154	(66.1)	
M2	21	(7.9)	18	(7.7)	
extra.ica (mean (sd))	0.26	(0.44)	0.32	(0.47)	0.150
time.rand (mean (sd))	213.88	(70.29)	202.51	(57.33)	0.051

1.4.1 Some of this is very useful, and other parts need to be fixed.

- 1. The 1/0 variables (afib, dm, extra.ica) might be better if they were treated as the factors they are, and reported as the Yes/No variables are reported, with counts and percentages rather than with means and standard deviations.
- 2. In some cases, we may prefer to re-order the levels of the categorical (factor) variables, particularly the mrankin variable, but also the ia.occlus variable. It would also be more typical to put the Intervention group to the left and the Control group to the right, so we may need to adjust our trt variable's levels accordingly.
- 3. For each of the quantitative variables (age, nihss, sbp, time.iv, aspects, extra.ica, time.rand and time.punc) we should make a decision whether a summary with mean and standard deviation is appropriate, or whether we should instead summarize with, say, the median and quartiles. A mean and standard deviation really only yields an appropriate summary when the data are least approximately Normally distributed. This will make the p values a bit more reasonable, too. The test column in the first attempt will soon have something useful to tell us.
- 4. If we'd left in the time.punc variable, we'd get some warnings, having to do with the fact that time.punc is only relevant to patients in the Intervention group.

1.4.2 fakestroke Cleaning Up Categorical Variables

Let's specify each of the categorical variables as categorical explicitly. This helps the CreateTableOne function treat them appropriately, and display them with counts and percentages. This includes all of the 1/0, Yes/No and multi-categorical variables.

Then we simply add a factorVars = fs.factorvars call to the CreateTableOne function.

We also want to re-order some of those categorical variables, so that the levels are more useful to us. Specifically, we want to:

- place Intervention before Control in the trt variable,
- reorder the mrankin scale as 0, 1, 2, > 2, and

• rearrange the ia.occlus variable to the order⁴ presented in Berkhemer et al. (2015).

To accomplish this, we'll use the fct_relevel function from the forcats package (loaded with the rest of the core tidyverse packages) to reorder our levels manually.

1.5 fakestroke Table 1: Attempt 2

;						
	Interve	ention	Control	L	p	test
n	233		267			
age (mean (sd))	63.93	(18.09)	65.38	(16.10)	0.343	
sex = Male (%)		(57.9)		(58.8)		
nihss (mean (sd))	17.97	(5.04)	18.08	(4.32)	0.787	
<pre>location = Right (%)</pre>	117	(50.2)	114	(42.7)	0.111	
hx.isch = Yes (%)	29	(12.4)	25	(9.4)	0.335	
afib = 1 (%)	66	(28.3)	69	(25.8)	0.601	
dm = 1 (%)	29	(12.4)	34	(12.7)	1.000	
mrankin (%)					0.922	
0	190	(81.5)	214	(80.1)		
1		(9.0)				
2	12	(5.2)	13	(4.9)		
> 2	10	(4.3)	11	(4.1)		
sbp (mean (sd))	146.03	(26.00)	145.00	(24.40)	0.647	
iv.altep = Yes (%)	203	(87.1)	242	(90.6)	0.267	
time.iv (mean (sd))	98.22	(45.48)	87.96	(26.01)	0.003	
aspects (mean (sd))	8.35	(1.64)	8.65	(1.47)	0.033	
ia.occlus (%)					0.795	
Intracranial ICA	1	(0.4)	3	(1.1)		
ICA with M1	59	(25.3)	75	(28.2)		
M1	154	(66.1)	165	(62.0)		
M2	18	(7.7)	21	(7.9)		
A1 or A2	1	(0.4)	2	(0.8)		
extra.ica = 1 (%)	75	(32.2)	70	(26.3)	0.179	
<pre>time.rand (mean (sd))</pre>	202.51	(57.33)	213.88	(70.29)	0.051	

The categorical data presentation looks much improved.

⁴We might also have considered reordering the ia.occlus factor by its frequency, using the fct_infreq function

1.5.1 What summaries should we show?

Now, we'll move on to the issue of making a decision about what type of summary to show for the quantitative variables. Since the fakestroke data are just simulated and only match the summary statistics of the original results, not the details, we'll adopt the decisions made by Berkhemer et al. (2015), which were to use medians and interquartile ranges to summarize the distributions of all of the continuous variables except systolic blood pressure.

- Specifying certain quantitative variables as *non-normal* causes R to show them with medians and the 25th and 75th percentiles, rather than means and standard deviations, and also causes those variables to be tested using non-parametric tests, like the Wilcoxon signed rank test, rather than the t test. The test column indicates this with the word nonnorm.
 - In real data situations, what should we do? The answer is to look at the data. I would not make the decision as to which approach to take without first plotting (perhaps in a histogram or a Normal Q-Q plot) the observed distributions in each of the two samples, so that I could make a sound decision about whether Normality was a reasonable assumption. If the means and medians are meaningfully different from each other, this is especially important.
 - To be honest, though, if the variable in question is a relatively unimportant covariate and the p values for the two approaches are nearly the same, I'm not sure that further investigation is especially important,
- Specifying *exact* tests for certain categorical variables (we'll try this for the location and mrankin variables) can be done, and these changes will be noted in the test column, as well.
 - In real data situations, I would rarely be concerned about this issue, and often choose Pearson (approximate) options across the board. This is reasonable so long as the number of subjects falling in each category is reasonably large, say above 10. If not, then an exact test may be an improvement.

To accomplish the Table 1, then, we need to specify which variables should be treated as non-Normal in the print statement - notice that we don't need to redo the CreateTableOne for this change.

	Stratifi	ied by trt		
	Interve	ention	Control	L
n	233		267	
age (median [IQR])	65.80	[54.50, 76.00]	65.70	[55.75, 76.20]
sex = Male (%)	135	(57.9)	157	(58.8)
nihss (median [IQR])	17.00	[14.00, 21.00]	18.00	[14.00, 22.00]
location = Right (%)	117	(50.2)	114	(42.7)
hx.isch = Yes (%)	29	(12.4)	25	(9.4)
afib = 1 (%)	66	(28.3)	69	(25.8)
dm = 1 (%)	29	(12.4)	34	(12.7)
mrankin (%)				
0	190	(81.5)	214	(80.1)
1	21	(9.0)	29	(10.9)
2	12	(5.2)	13	(4.9)
> 2	10	(4.3)	11	(4.1)
sbp (mean (sd))	146.03	(26.00)	145.00	(24.40)
<pre>iv.altep = Yes (%)</pre>	203	(87.1)	242	(90.6)
time.iv (median [IQR])	85.00	[67.00, 110.00]	87.00	[65.00, 116.00]
aspects (median [IQR])	9.00	[7.00, 10.00]	9.00	[8.00, 10.00]
ia.occlus (%)				
Intracranial ICA	1	(0.4)	3	(1.1)
ICA with M1	59	(25.3)	75	(28.2)

```
M1
                             154 (66.1)
                                                      165 (62.0)
                              18 (7.7)
  M2
                                                       21 (7.9)
   A1 or A2
                               1 (0.4)
                                                       2 (0.8)
                              75 (32.2)
extra.ica = 1 (\%)
                                                       70 (26.3)
time.rand (median [IQR]) 204.00 [152.00, 249.50] 196.00 [149.00, 266.00]
                        Stratified by trt
                                 test
age (median [IQR])
                           0.579 nonnorm
                           0.917
sex = Male (%)
nihss (median [IQR])
                           0.453 nonnorm
location = Right (%)
                           0.106 exact
hx.isch = Yes (%)
                           0.335
afib = 1 (%)
                           0.601
dm = 1 (\%)
                           1.000
mrankin (%)
                           0.917 exact
   0
   1
   2
   > 2
sbp (mean (sd))
                           0.647
iv.altep = Yes (%)
                           0.267
time.iv (median [IQR])
                           0.596 nonnorm
aspects (median [IQR])
                           0.075 nonnorm
                           0.795
ia.occlus (%)
   Intracranial ICA
   ICA with M1
   M1
   M2
   A1 or A2
extra.ica = 1 (\%)
                           0.179
time.rand (median [IQR]) 0.251 nonnorm
```

1.6 Obtaining a more detailed Summary

summary(att2)

If this was a real data set, we'd want to get a more detailed description of the data to make decisions about things like potentially collapsing categories of a variable, or whether or not a normal distribution was useful for a particular continuous variable, etc. You can do this with the summary command applied to a created Table 1, which shows, among other things, the effect of changing from normal to non-normal p values for continuous variables, and from approximate to "exact" p values for categorical factors.

Again, as noted above, in a real data situation, we'd want to plot the quantitative variables (within each group) to make a smart decision about whether a t test or Wilcoxon approach is more appropriate.

Note in the summary below that we have some missing values here. Often, we'll present this information within the Table 1, as well.

```
### Summary of continuous variables ###
trt: Intervention
```

n miss p.miss mean sd median p25 p75 min max skew kurt

age	233	0	0.0	64	18	66	54	76	23	96	-0.34	-0.52
nihss	233	0	0.0	18	5	17	14	21	10	28	0.48	-0.74
sbp	233	0	0.0	146	26	146	129	164	78	214	-0.07	-0.22
time.iv	233	30	12.9	98	45	85	67	110	42	218	1.03	0.08
aspects	233	0	0.0	8	2	9	7	10	5	10	-0.56	-0.98
time.rand	233	2	0.9	203	57	204	152	250	100	300	0.01	-1.16

trt: Control

	n	miss	p.miss	${\tt mean}$	sd	${\tt median}$	p25	p75	\min	${\tt max}$	skew	kurt
age	267	0	0.0	65	16	66	56	76	24	94	-0.296	-0.28
nihss	267	0	0.0	18	4	18	14	22	11	25	0.017	-1.24
sbp	267	1	0.4	145	24	145	128	161	82	231	0.156	0.08
time.iv	267	25	9.4	88	26	87	65	116	44	130	0.001	-1.32
aspects	267	4	1.5	9	1	9	8	10	5	10	-1.071	0.36
time.rand	267	0	0.0	214	70	196	149	266	120	360	0.508	-0.93

p-values

pNormal pNonNormal age 0.342813660 0.57856976 nihss 0.787487252 0.45311695 sbp 0.647157646 0.51346132 time.iv 0.003073372 0.59641104 aspects 0.032662901 0.07464683 time.rand 0.050803672 0.25134327

Standardize mean differences

1 vs 2

age 0.08478764
nihss 0.02405390
sbp 0.04100833
time.iv 0.27691223
aspects 0.19210662
time.rand 0.17720957

Summary of categorical variables

trt: Intervention

crc. incerv	ent.	LOII					
var	n	${\tt miss}$	p.miss	level	freq	percent	cum.percent
sex	233	0	0.0	Female	98	42.1	42.1
				Male	135	57.9	100.0
location	233	0	0.0	Left	116	49.8	49.8
				Right	117	50.2	100.0
hx.isch	233	0	0.0	No	204	87.6	87.6
				Yes	29	12.4	100.0
afib	233	0	0.0	0	167	71.7	71.7
0110				1	66	28.3	100.0
dm	233	0	0.0	0	204	87.6	87.6
				1	29	12.4	100.0

mrankin	233	0	0.0	0 1 2 > 2		81.5 9.0 5.2 4.3	
iv.altep	233	0	0.0	No Yes	30 203	12.9	12.9
ia.occlus	233	0	0.0	Intracranial ICA ICA with M1 M1 M2 A1 or A2	59 154 18	25.3 66.1 7.7	25.8 91.8 99.6
extra.ica	233	0	0.0		158 75	67.8 32.2	
trt: Contro	 ol						
var	n	miss	p.miss	level	freq	percent	cum.percent
			0.0		-	-	41.2
				Male	157	58.8	100.0
location	267	0	0.0	Left	153	57.3	57.3
				Right			100.0
hx.isch	267	0	0.0	No	242	90.6	90.6
				Yes	25	9.4	100.0
afib	267	0	0.0	0	198	74.2	74.2
				1	69	25.8	
dm	267	0	0.0	0	233	87.3	87.3
Q.III	201	v	0.0	1			100.0
mrankin	267	0	0.0	0	214	80.1	80.1
				1	29	10.9	91.0
				2	13	4.9	95.9
				> 2	11	4.1	100.0
iv.altep	267	0	0.0	No	25	9.4	9.4
•				Yes	242	90.6	100.0
ia.occlus	267	1	0.4	Intracranial ICA	3	1.1	1.1
				ICA with M1	75	28.2	29.3
				M1	165	62.0	91.4
				M2	21	7.9	99.2
				A1 or A2	2	0.8	100.0
extra.ica	267	1	0.4	0	196	73.7	73.7
	•	_		1	70	26.3	100.0

```
p-values
           pApprox
                      pExact
         0.9171387 0.8561188
location 0.1113553 0.1056020
hx.isch 0.3352617 0.3124683
afib
         0.6009691 0.5460206
         1.0000000 1.0000000
mrankin 0.9224798 0.9173657
iv.altep 0.2674968 0.2518374
ia.occlus 0.7945580 0.8189090
extra.ica 0.1793385 0.1667574
Standardize mean differences
              1 vs 2
         0.017479025
sex
location 0.151168444
hx.isch 0.099032275
afib
         0.055906317
         0.008673478
mrankin 0.062543164
iv.altep 0.111897009
ia.occlus 0.117394890
extra.ica 0.129370206
```

In this case, I have simulated the data to mirror the results in the published Table 1 for this study. In no way have I captured the full range of the real data, or any of the relationships in that data, so it's more important here to see what's available in the analysis, rather than to interpret it closely in the clinical context.

1.7 Exporting the Completed Table 1 from R to Excel or Word

Once you've built the table and are generally satisfied with it, you'll probably want to be able to drop it into Excel or Word for final cleanup.

1.7.1 Approach A: Save and open in Excel

One option is to save the Table 1 to a .csv file, which you can then open directly in Excel. This is the approach I generally use. Note the addition of some quote, noSpaces and printToggle selections here.

When I then open the fs-table1.csv file in Excel, it looks like this:

4	Α	В	С	D	E
1		Intervention	Control	p	test
2	n	233	267		
3	age (median [IQR])	65.80 [54.50, 76.00]	65.70 [55.75, 76.20]	0.579	nonnorm
4	sex = Male (%)	135 (57.9)	157 (58.8)	0.917	
5	nihss (median [IQR])	17.00 [14.00, 21.00]	18.00 [14.00, 22.00]	0.453	nonnorm
6	location = Right (%)	117 (50.2)	114 (42.7)	0.111	
7	hx.isch = Yes (%)	29 (12.4)	25 (9.4)	0.335	
8	afib = 1 (%)	66 (28.3)	69 (25.8)	0.601	
9	dm = 1 (%)	29 (12.4)	34 (12.7)	1	
10	mrankin (%)			0.922	
11	0	190 (81.5)	214 (80.1)		
12	1	21 (9.0)	29 (10.9)		
13	2	12 (5.2)	13 (4.9)		
14	>2	10 (4.3)	11 (4.1)		
15	sbp (mean (sd))	146.03 (26.00)	145.00 (24.40)	0.647	
16	iv.altep = Yes (%)	203 (87.1)	242 (90.6)	0.267	
17	time.iv (median [IQR])	85.00 [67.00, 110.00]	87.00 [65.00, 116.00]	0.596	nonnorm
18	aspects (median [IQR])	9.00 [7.00, 10.00]	9.00 [8.00, 10.00]	0.075	nonnorm
19	ia.occlus (%)			0.795	
20	Intracranial ICA	1 (0.4)	3 (1.1)		
21	ICA with M1	59 (25.3)	75 (28.2)		
22	M1	154 (66.1)	165 (62.0)		
23	M2	18 (7.7)	21 (7.9)		
24	A1 or A2	1 (0.4)	2 (0.8)		
25	extra.ica = 1 (%)	75 (32.2)	70 (26.3)	0.179	
26	time.rand (median [IQR])	204.00 [152.00, 249.50]	196.00 [149.00, 266.00]	0.251	nonnorm
27	time.punc (median [IQR])	260.00 [212.00, 313.00]	NA [NA, NA]	NA	nonnorm
28					

And from here, I can either drop it directly into Word, or present it as is, or start tweaking it to meet formatting needs.

1.7.2 Approach B: Produce the Table so you can cut and paste it

This will look like a mess by itself, but if you:

- 1. copy and paste that mess into Excel
- 2. select Text to Columns from the Data menu
- 3. select Delimited, then Space and select Treat consecutive delimiters as one

you should get something usable again.

Or, in Word,

1. insert the text

- 2. select the text with your mouse
- 3. select Insert ... Table ... Convert Text to Table
- 4. place a quotation mark in the "Other" area under Separate text at ...

After dropping blank columns, the result looks pretty good.

1.8 A Controlled Biological Experiment - The Blood-Brain Barrier

My source for the data and the following explanatory paragraph is page 307 from Ramsey and Schafer (2002). The original data come from Barnett et al. (1995).

The human brain (and that of rats, coincidentally) is protected from the bacteria and toxins that course through the bloodstream by something called the blood-brain barrier. After a method of disrupting the barrier was developed, researchers tested this new mechanism, as follows. A series of 34 rats were inoculated with human lung cancer cells to induce brain tumors. After 9-11 days they were infused with either the barrier disruption (BD) solution or, as a control, a normal saline (NS) solution. Fifteen minutes later, the rats received a standard dose of a particular therapeutic antibody (L6-F(ab')2. The key measure of the effectiveness of transmission across the brain-blood barrier is the ratio of the antibody concentration in the brain tumor to the antibody concentration in normal tissue outside the brain. The rats were then sacrificed, and the amounts of antibody in the brain tumor and in normal tissue from the liver were measured. The study's primary objective is to determine whether the antibody concentration in the tumor increased when the blood-barrier disruption infusion was given, and if so, by how much?

1.9 The bloodbrain.csv file

Consider the data, available on the Data and Code page of our course website in the bloodbrain.csv file, which includes the following variables:

Variable	Description
case	identification number for the rat (1 - 34)
brain	an outcome: Brain tumor antibody count (per gram)
liver	an outcome: Liver antibody count (per gram)
tlratio	an outcome: tumor / liver concentration ratio
solution	the treatment: BD (barrier disruption) or NS (normal saline)
sactime	a design variable: Sacrifice time (hours; either 0.5, 3, 24 or 72)
postin	covariate: Days post-inoculation of lung cancer cells (9, 10 or
	11)
sex	covariate: M or F
wt.init	covariate: Initial weight (grams)
wt.loss	covariate: Weight loss (grams)
wt.tumor	covariate: Tumor weight (10 ⁻⁴ grams)

And here's what the data look like in R.

bloodbrain

```
# A tibble: 34 x 11

case brain liver tlratio solution sactime postin sex wt.init
<int> <int> <int> <int> <fct> <fct> <dbl> <fct> <dbl> <int> <fct> <int> 239
```

```
2 44286 1602171 0.0276 BD
                                           0.500
                                                     10 F
                                                                  225
 3
      3 102926 1601936 0.0642 BD
                                           0.500
                                                     10 F
                                                                  224
                                                     10 F
 4
      4 25927 1776411 0.0146 BD
                                           0.500
                                                                  184
 5
      5 42643 1351184 0.0316 BD
                                           0.500
                                                     10 F
                                                                  250
 6
      6
         31342 1790863 0.0175 NS
                                           0.500
                                                     10 F
                                                                  196
7
                                           0.500
      7 22815 1633386 0.0140 NS
                                                     10 F
                                                                  200
                                           0.500
8
        16629 1618757 0.0103 NS
                                                     10 F
                                                                  273
9
      9
         22315 1567602 0.0142 NS
                                           0.500
                                                     10 F
                                                                  216
     10
         77961 1060057 0.0735 BD
                                           3.00
                                                     10 F
                                                                  267
# ... with 24 more rows, and 2 more variables: wt.loss <dbl>, wt.tumor
    <int>
```

1.10 A Table 1 for bloodbrain

Barnett et al. (1995) did not provide a Table 1 for these data, so let's build one to compare the two solutions (BD vs. NS) on the covariates and outcomes, plus the natural logarithm of the tumor/liver concentration ratio (tlratio). We'll opt to treat the sacrifice time (sactime) and the days post-inoculation of lung cancer cells (postin) as categorical rather than quantitative variables.

Summary of continuous variables

```
solution: BD
                                              p25
         n miss p.miss
                         mean
                                  sd median
                                                    p75
                                                            min
                                                                  max
wt.init
        17
              0
                          243 3e+01
                                     2e+02
                                            2e+02 3e+02
                                                         2e+02 3e+02
wt.loss 17
              0
                     0
                             3 5e+00
                                     4e+00
                                            1e+00 6e+00 -5e+00 1e+01
wt.tumor 17
              0
                     0
                          157 8e+01
                                     2e+02
                                            1e+02 2e+02
                                                         2e+01 4e+02
              0
                     0 56043 3e+04 5e+04 4e+04 8e+04
                                                         6e+03 1e+05
brain
         17
                     0 672577 7e+05 6e+05 2e+04 1e+06
                                                         2e+03 2e+06
liver
         17
              0
                            2 3e+00 1e-01 6e-02 3e+00 1e-02 9e+00
tlratio
        17
              0
                     0
logTL
               0
                           -1 2e+00 -2e+00 -3e+00 1e+00 -4e+00 2e+00
         17
         skew kurt
wt.init -0.39 0.7
wt.loss -0.10 0.2
```

```
wt.tumor 0.53 1.0
brain 0.29 -0.6
                0.35 - 1.7
liver
tlratio 1.58 1.7
logTL 0.08 -1.7
 -----
solution: NS
                   n miss p.miss mean sd median p25 p75 min max
wt.init 17 0 0 240 3e+01 2e+02 2e+02 3e+02 2e+02 3e+02

      wt.lnit
      17
      0
      0
      240 Se+01
      2e+02
      2e+02
      3e+02
      2e+02
      3e+02
      2e+02
      3e+02
      2e+02
      3e+02
      3e+01
      5e+02
      3e+02
      3e+02
      3e+01
      5e+02
      3e+02
      3e+01
      5e+02
      3e+02
      3e+01
      3e+02
      3e+01
      3e+02
      3e+04
      1e+03
      5e+04
      1e+03
      5e+04
      1e+03
      5e+04
      1e+06
      9e+02
      2e+06
      1e+03
      5e+02
      3e+02
      3e+0
                   skew kurt
wt.init 0.33 -0.48
wt.loss -0.09 0.08
wt.tumor 0.63 0.77
brain 0.30 -0.35
liver
                 0.40 - 1.56
tlratio 2.27 4.84
logTL
                0.27 - 1.61
p-values
                          pNormal pNonNormal
wt.init 0.807308940 0.641940278
wt.loss 0.683756156 0.876749808
wt.tumor 0.151510151 0.190482094
brain 0.001027678 0.002579901
liver
                  0.974853609 0.904045603
tlratio 0.320501715 0.221425879
logTL
                 0.351633525 0.221425879
Standardize mean differences
                          1 vs 2
wt.init 0.08435244
wt.loss 0.14099823
wt.tumor 0.50397184
brain 1.23884159
liver 0.01089667
tlratio 0.34611465
logTL 0.32420504
          ### Summary of categorical variables ###
solution: BD
```

```
var n miss p.miss level freq percent cum.percent sactime 17 0 0.0 0.5 5 29.4 29.4 3 4 23.5 52.9 24 4 23.5 76.5 72 4 23.5 100.0
```

postin	17	0	0.0	9	1	5.9	5.9
				10	14	82.4	88.2
				11	2	11.8	100.0
	4.7	•	0 0	_	4.0	70.5	70.5
sex	17	0	0.0	F	13	76.5	76.5
				M	4	23.5	100.0
solution	: NS	3					
var	n	miss	p.miss	level	freq	percent	cum.percent
sactime	17	0	0.0	0.5	4	23.5	23.5
				3	5	29.4	52.9
				24	4	23.5	76.5
				72	4	23.5	100.0
postin	17	0	0.0	9	2	11.8	11.8
				10	13	76.5	88.2
				11	2	11.8	100.0
sex	17	0	0.0	F	13	76.5	76.5
				M	4	23.5	100.0

p-values

pApprox pExact sactime 0.9739246 1 postin 0.8309504 1 sex 1.0000000 1

Standardize mean differences

1 vs 2 sactime 0.1622214 postin 0.2098877 sex 0.0000000

Note that, in this particular case, the decisions we make about normality vs. non-normality (for quantitative variables) and the decisions we make about approximate vs. exact testing (for categorical variables) won't actually change the implications of the p values. Each approach gives similar results for each variable. Of course, that's not always true.

1.10.1 Generate final Table 1 for bloodbrain

I'll choose to treat tlratio and its logarithm as non-Normal, but otherwise, use t tests, but admittedly, that's an arbitrary decision, really.

print(bb.att1, nonnormal = c("tlratio", "logTL"))

	Stratified by solution	n
	BD	NS
n	17	17
<pre>sactime (%)</pre>		
0.5	5 (29.4)	4 (23.5)
3	4 (23.5)	5 (29.4)
24	4 (23.5)	4 (23.5)

```
72
                                                         4 (23.5)
                                4 (23.5)
postin (%)
   9
                                1 (5.9)
                                                         2 (11.8)
   10
                               14 (82.4)
                                                        13 (76.5)
   11
                                2 (11.8)
                                                         2 (11.8)
sex = M (\%)
                                4 (23.5)
                                                         4 (23.5)
wt.init (mean (sd))
                           242.82 (27.23)
                                                    240.47 (28.54)
wt.loss (mean (sd))
                                                      3.94 (3.88)
                             3.34 (4.68)
wt.tumor (mean (sd))
                           157.29 (84.00)
                                                    208.53 (116.68)
brain (mean (sd))
                         56043.41 (33675.40)
                                                  23887.18 (14610.53)
liver (mean (sd))
                        672577.35 (694479.58)
                                                 664975.47 (700773.13)
tlratio (median [IQR])
                             0.12 [0.06, 2.84]
                                                      0.05 [0.03, 0.94]
logTL (median [IQR])
                            -2.10 [-2.74, 1.04]
                                                     -2.95 [-3.41, -0.07]
                       Stratified by solution
                               test
sactime (%)
                         0.974
   0.5
   3
   24
   72
postin (%)
                         0.831
   9
   10
   11
sex = M (\%)
                         1.000
wt.init (mean (sd))
                         0.807
wt.loss (mean (sd))
                         0.684
wt.tumor (mean (sd))
                         0.152
brain (mean (sd))
                         0.001
liver (mean (sd))
                         0.975
tlratio (median [IQR])
                        0.221 nonnorm
logTL (median [IQR])
                         0.221 nonnorm
```

Or, we can get an Excel-readable version, using

A	A	В	С	D	E
1		BD	NS	р	test
2	n	17	17		
3	sex = M (%)	4 (23.5)	4 (23.5)	1	
4	sactime (%)			0.974	
5	0.5	5 (29.4)	4 (23.5)		
6	3	4 (23.5)	5 (29.4)		
7	24	4 (23.5)	4 (23.5)		
8	72	4 (23.5)	4 (23.5)		
9	postin (%)			0.831	
10	9	1 (5.9)	2 (11.8)		
11	10	14 (82.4)	13 (76.5)		
12	11	2 (11.8)	2 (11.8)		
13	wt.init (mean (sd))	242.82 (27.23)	240.47 (28.54)	0.807	
14	wt.loss (mean (sd))	3.34 (4.68)	3.94 (3.88)	0.684	
15	wt.tumor (mean (sd))	157.29 (84.00)	208.53 (116.68)	0.152	
16	brain (mean (sd))	56043.41 (33675.40)	23887.18 (14610.53)	0.001	
17	liver (mean (sd))	672577.35 (694479.58)	664975.47 (700773.13)	0.975	
18	tlratio (median [IQR])	0.12 [0.06, 2.84]	0.05 [0.03, 0.94]	0.221	nonnorm
19	logTL (median [IQR])	-2.10 [-2.74, 1.04]	-2.95 [-3.41, -0.07]	0.221	nonnorm
20					

One thing I would definitely clean up here, in practice, is to change the presentation of the p value for sex from 1 to > 0.99, or just omit it altogether. I'd also drop the computer-ese where possible, add units for the measures, round a lot, identify the outcomes carefully, and use notes to indicate deviations from the main approach.

1.10.2 A More Finished Version (after Cleanup in Word)

Table 1. Comparing Rats Receiving BD to those Receiving NS on Available Covariates and Design Variables, and Key Outcomes

	Barrier Disruption	Normal Saline	
	(BD: treatment)	(NS: control)	р
# of Rats	17	17	
Sex = Male	4 (23.5)	4 (23.5)	-
Sacrifice Time (hours)			0.97
0.5	5 (29.4)	4 (23.5)	
3	4 (23.5)	5 (29.4)	
24	4 (23.5)	4 (23.5)	
72	4 (23.5)	4 (23.5)	
Days post-inoculation of			0.83
lung cancer cells			0.03
9	1 (5.9)	2 (11.8)	
10	14 (82.4)	13 (76.5)	
11	2 (11.8)	2 (11.8)	
Initial Weight (g)	243 (27)	240 (29)	0.81
Weight Loss (g)	3.3 (4.7)	3.9 (3.9)	0.68
Tumor Weight (10 ⁻⁴ g)	157.3 (84.0)	208.5 (116.7)	0.15
Key Outcomes: mean (sd) unless otherw	ise indicated		
Brain Tumor Antibody Count (per g)	56,043 (33,675)	23,887 (14,611)	0.001
Liver Antibody Count (per g)	672,577 (694,480)	664,975 (700,773)	0.98
Tumor/Liver Ratio	0.12	0.05	0.22
(median [Q25, Q75])	[0.06, 2.84]	[0.03, 0.94]	0.22
Natural Log of Tumor/Liver Ratio	-2.10	-2.95	0.22
(median [Q25, Q75])	[-2.74, 1.04]	[-3.41, -0.07]	0.22

Table 1 Notes:

- Categorical variables are summarized with counts, percentages and p values based on approximate chi-square tests.
- Continuous variables, unless otherwise indicated, are summarized with means, standard deviations and p values based on t tests.
- The Tumor / Liver ratio and its natural logarithm are summarized with the median and quartiles and a p value from a non-parametric (Wilcoxon signed rank) test.

Chapter 2

Linear Regression on a small SMART data set

2.1 BRFSS and SMART

The Centers for Disease Control analyzes Behavioral Risk Factor Surveillance System (BRFSS) survey data for specific metropolitan and micropolitan statistical areas (MMSAs) in a program called the Selected Metropolitan/Micropolitan Area Risk Trends of BRFSS (SMART BRFSS.)

In this work, we will focus on data from the 2016 SMART, and in particular on data from the Cleveland-Elyria, OH, Metropolitan Statistical Area. The purpose of this survey is to provide localized health information that can help public health practitioners identify local emerging health problems, plan and evaluate local responses, and efficiently allocate resources to specific needs.

2.1.1 Key resources

- the full data are available in the form of the 2016 SMART BRFSS MMSA Data, found in a zipped SAS Transport Format file. The data were released in August 2017.
- the MMSA Variable Layout PDF which simply lists the variables included in the data file
- the Calculated Variables PDF which describes the risk factors by data variable names there is also an online summary matrix of these calculated variables, as well.
- the lengthy 2016 Survey Questions PDF which lists all questions asked as part of the BRFSS in 2016
- the enormous Codebook for the 2016 BRFSS Survey PDF which identifies the variables by name for

Later this term, we'll use all of those resources to help construct a more complete data set than we'll study today. I'll also demonstrate how I built the smartcle1 data set that we'll use in this Chapter.

2.2 The smartcle1 data: Cookbook

The smartcle1.csv data file available on the Data and Code page of our website describes information on 11 variables for 1036 respondents to the BRFSS 2016, who live in the Cleveland-Elyria, OH, Metropolitan Statistical Area. The variables in the smartcle1.csv file are listed below, along with (in some cases) the BRFSS items that generate these responses.

Variable	Description
SEQNO	respondent identification number (all begin with 2016)

Variable	Description
physhealth	Now thinking about your physical health, which includes physical illness and injury, for how many days during the past 30 days was your physical health not good?
menthealth	Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?
poorhealth	During the past 30 days, for about how many days did poor physical or mental health keep you from doing your usual activities, such as self-care, work, or recreation?
genhealth	Would you say that in general, your health is (five categories: Excellent, Very Good, Good, Fair or Poor)
bmi	Body mass index, in kg/m ²
female	Sex, $1 = \text{female}$, $0 = \text{male}$
internet30	Have you used the internet in the past 30 days? $(1 = yes, 0 = no)$
exerany	During the past month, other than your regular job, did you participate in any physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise? $(1 = yes, 0 = no)$
sleephrs	On average, how many hours of sleep do you get in a 24-hour period?
alcdays	How many days during the past 30 days did you have at least one drink of any alcoholic beverage such as beer, wine, a malt beverage or liquor?

str(smartcle1)

```
Classes 'tbl_df', 'tbl' and 'data.frame': 1036 obs. of 11 variables:

$ SEQNO : num 2.02e+09 2.02e+09 2.02e+09 2.02e+09 2.02e+09 ...

$ physhealth: int 0 0 1 0 5 4 2 2 0 0 ...

$ menthealth: int 0 0 5 0 0 18 0 3 0 0 ...

$ poorhealth: int NA NA 0 NA 0 6 0 0 NA NA ...

$ genhealth : Factor w/ 5 levels "1_Excellent",..: 2 1 2 3 1 2 3 3 2 3 ...

$ bmi : num 26.7 23.7 26.9 21.7 24.1 ...

$ female : int 1 0 0 1 0 0 1 1 0 0 ...

$ internet30: int 1 1 1 1 1 1 1 1 1 ...

$ exerany : int 1 1 0 1 1 1 1 1 0 ...

$ sleephrs : int 6 6 8 9 7 5 9 7 7 7 ...

$ alcdays : int 1 4 4 3 2 28 4 2 4 25 ...
```

2.3 smartcle2: Omitting Missing Observations: Complete-Case Analyses

For the purpose of fitting our first few models, we will eliminate the missingness problem, and look only at the *complete cases* in our smartcle1 data.

To inspect the missingness in our data, we might consider using the skim function from the skimr package. We'll exclude the respondent identifier code (SEQNO) from this summary as uninteresting.

```
skim_with(numeric = list(hist = NULL), integer = list(hist = NULL))
## above line eliminates the sparkline histograms
## it can be commented out when working in the console,
## but I need it to produce the Notes without errors right now
```

```
smartcle1 %>%
   skim(-SEQNO)
Skim summary statistics
n obs: 1036
n variables: 11
Variable type: factor
 variable missing complete
                             n n_unique
genhealth
                      1033 1036
                3
                            top_counts ordered
2_V: 350, 3_G: 344, 1_E: 173, 4_F: 122
Variable type: integer
  variable missing complete
                                       sd p0 p25 median p75 p100
                               n mean
   alcdays
              46 990 1036 4.65 8.05
   exerany
                3
                      1033 1036 0.76 0.43 0
                                               1
                                                               1
    female
                0
                      1036 1036 0.6 0.49 0
                                               0
                                                          1
                                                               1
internet30
                6
                       1030 1036 0.81 0.39 0
                                               1
                                                      1
                                                          1
                                                               1
menthealth
               11
                       1025 1036 2.72 6.82 0
                                                              30
                       1019 1036 3.97 8.67 0
                                                          2
physhealth
               17
                                                      0
                                                              30
                                               0
poorhealth
               543
                       493 1036 4.07 8.09 0
                                                              30
  sleephrs
                 8
                       1028 1036 7.02 1.53 1
                                                              20
Variable type: numeric
variable missing complete
                             n mean
                                       sd
                                            p0 p25 median
                                                             p75 p100
                      952 1036 27.89 6.47 12.71 23.7 26.68 30.53 66.06
     bmi
```

Now, we'll create a new tibble called smartcle2 which contains every variable except poorhealth, and which includes all respondents with complete data on the variables (other than poorhealth). We'll store those observations with complete data in the smartcle2 tibble.

```
smartcle2 <- smartcle1 %>%
    select(-poorhealth) %>%
    filter(complete.cases(.))
smartcle2
```

A tibble: 896 x 10

	SEQNO	phy shealth	${\tt menthealth}$	genhealth	bmi	female	${\tt internet30}$	exerany
	<dbl></dbl>	<int></int>	<int></int>	<fct></fct>	<dbl></dbl>	<int></int>	<int></int>	<int></int>
1	2.02e9	0	0	2_VeryGo~	26.7	1	1	1
2	2.02e9	0	0	1_Excell~	23.7	0	1	1
3	2.02e9	1	5	2_VeryGo~	26.9	0	1	0
4	2.02e9	0	0	3_Good	21.7	1	1	1
5	2.02e9	5	0	1_Excell~	24.1	0	1	1
6	2.02e9	4	18	2_VeryGo~	27.6	0	1	1
7	2.02e9	2	0	3_Good	25.7	1	1	1
8	2.02e9	2	3	3_Good	28.5	1	1	1
9	2.02e9	0	0	2_VeryGo~	28.6	0	1	1
10	2.02e9	0	0	3_Good	23.1	0	1	0
ш		006				. 7		

... with 886 more rows, and 2 more variables: sleephrs <int>, alcdays

<int>

Note that there are only 896 respondents with **complete** data on the 10 variables (excluding **poorhealth**) in the **smartcle2** tibble, as compared to our original **smartcle1** data which described 1036 respondents and

11 variables, but with lots of missing data.

2.4 Summarizing the smartcle2 data numerically

2.4.1 The New Toy: The skim function

```
skim(smartcle2, -SEQNO)
Skim summary statistics
n obs: 896
n variables: 10
Variable type: factor
 variable missing complete
                             n n_unique
genhealth
                       896 896
                            top_counts ordered
2_V: 306, 3_G: 295, 1_E: 155, 4_F: 102
Variable type: integer
  variable missing complete
                                       sd p0 p25 median p75 p100
                              n mean
               0
                        896 896 4.83 8.14
                                               0
   alcdays
                 0
   exerany
                        896 896 0.77 0.42 0
                                               1
                                                      1
    female
                 0
                        896 896 0.58 0.49 0
 internet30
                 0
                        896 896 0.81 0.39 0
                                               1
                                                               1
menthealth
                 0
                        896 896 2.69 6.72 0
                                                      0
                                                              30
                 0
                        896 896 3.99 8.64 0
                                                      0 2
                                                              30
physhealth
                        896 896 7.02 1.48 1
  sleephrs
                 0
Variable type: numeric
                                            p0 p25 median
variable missing complete
                            n mean
                                      sd
                                                             p75 p100
                      896 896 27.87 6.33 12.71 23.7
                                                      26.8 30.53 66.06
     bmi
```

2.4.2 The usual summary for a data frame

Of course, we can use the usual summary to get some basic information about the data.

summary(smartcle2)

```
SEQNO
                     physhealth
                                    menthealth
                                                        genhealth
Min.
      :2.016e+09
                  Min. : 0.00
                                  Min. : 0.000 1_Excellent:155
                   1st Qu.: 0.00
                                  1st Qu.: 0.000
1st Qu.:2.016e+09
                                                  2_VeryGood:306
Median :2.016e+09
                   Median: 0.00
                                  Median : 0.000
                                                  3_{Good}
                                                             :295
     :2.016e+09
                   Mean
                         : 3.99
                                  Mean
                                        : 2.693
                                                  4_Fair
                                                             :102
                                                             : 38
3rd Qu.:2.016e+09
                   3rd Qu.: 2.00
                                  3rd Qu.: 2.000
                                                  5_Poor
      :2.016e+09
                  Max. :30.00
                                  Max.
                                         :30.000
Max.
                   female
                                 internet30
    bmi
                                                  exerany
               Min. :0.0000 Min. :0.0000
                                                      :0.0000
Min.
      :12.71
                                               Min.
1st Qu.:23.70 1st Qu.:0.0000
                              1st Qu.:1.0000
                                               1st Qu.:1.0000
Median :26.80
               Median :1.0000
                               Median :1.0000
                                               Median :1.0000
Mean :27.87
               Mean :0.5848
                               Mean :0.8147
                                               Mean
                                                      :0.7667
3rd Qu.:30.53
               3rd Qu.:1.0000
                               3rd Qu.:1.0000
                                               3rd Qu.:1.0000
Max. :66.06
                     :1.0000
                              Max. :1.0000
                                                      :1.0000
               Max.
                                               {\tt Max.}
```

```
      sleephrs
      alcdays

      Min. : 1.000
      Min. : 0.000

      1st Qu.: 6.000
      1st Qu.: 0.000

      Median : 7.000
      Median : 1.000

      Mean : 7.022
      Mean : 4.834

      3rd Qu.: 8.000
      3rd Qu.: 5.000

      Max. : 20.000
      Max. : 30.000
```

2.4.3 The describe function in Hmisc

Or we can use the ${\tt describe}$ function from the ${\tt Hmisc}$ package.

```
Hmisc::describe(select(smartcle2, bmi, genhealth, female))
select(smartcle2, bmi, genhealth, female)
                 896 Observations
 3 Variables
      n missing distinct Info Mean Gmd .05 .10
896 0 467 1 27.87 6.572 20.06 21.23
.25 .50 .75 .90 .95
      . 25
   23.70 26.80 30.53 35.36 39.30
lowest: 12.71 13.34 14.72 16.22 17.30, highest: 56.89 57.04 60.95 61.84 66.06
______
genhealth
       n missing distinct
      896 0 5

      Value
      1_Excellent
      2_VeryGood
      3_Good
      4_Fair

      Frequency
      155
      306
      295
      102

      Proportion
      0.173
      0.342
      0.329
      0.114

                                                                            38
                                                                            0.042
     n missing distinct Info Sum Mean Gmd 896 0 2 0.728 524 0.5848 0.4862
```

2.5 Counting as exploratory data analysis

Counting things can be amazingly useful.

2.5.1 How many respondents had exercised in the past 30 days? Did this vary by sex?

```
7.14
1
                 0
                       64
2
        0
                 1
                      308
                             34.4
3
        1
                 0
                      145
                             16.2
4
                             42.3
        1
                 1
                      379
```

so we know now that 42.3% of the subjects in our data were women who exercised. Suppose that instead we want to find the percentage of exercisers within each sex...

```
smartcle2 %>%
    count(female, exerany) %>%
   group_by(female) %>%
   mutate(prob = 100*n / sum(n))
# A tibble: 4 x 4
# Groups: female [2]
  female exerany
                     n prob
   <int>
           <int> <int> <dbl>
               0
                    64 17.2
1
       0
2
                   308 82.8
       0
               1
3
       1
               0
                   145
                       27.7
                   379 72.3
               1
```

and now we know that 82.8% of the males exercised at least once in the last 30 days, as compared to 72.3% of the females.

2.5.2 What's the distribution of sleephrs?

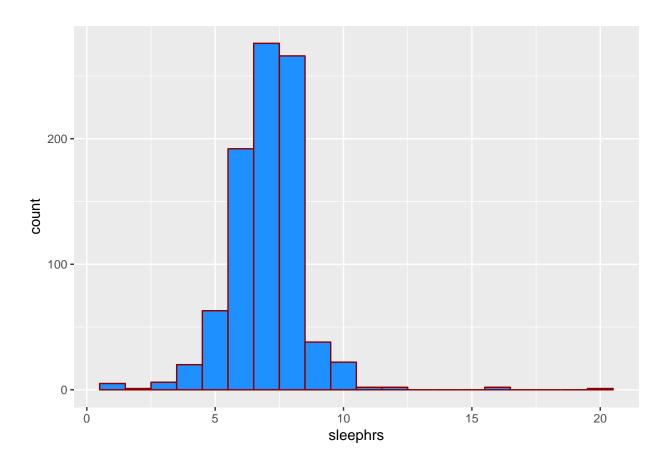
We can count quantitative variables with discrete sets of possible values, like sleephrs, which is captured as an integer (that must fall between 0 and 24.)

```
smartcle2 %>% count(sleephrs)
```

```
# A tibble: 14 x 2
   sleephrs
                  n
      <int> <int>
 1
           1
                  5
 2
           2
                  1
 3
           3
                  6
 4
           4
                 20
 5
           5
                 63
 6
           6
                192
7
           7
                276
8
           8
                266
9
           9
                 38
10
          10
                 22
                  2
          11
11
12
          12
                  2
13
          16
                  2
14
          20
```

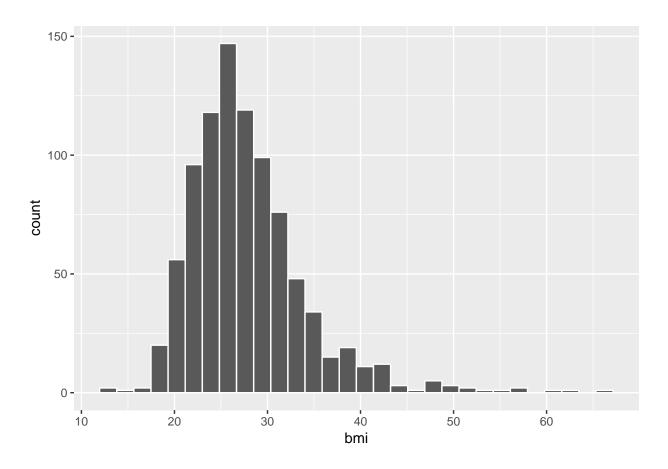
Of course, a natural summary of a quantitative variable like this would be graphical.

```
ggplot(smartcle2, aes(sleephrs)) +
  geom_histogram(binwidth = 1, fill = "dodgerblue", col = "darkred")
```



2.5.3 What's the distribution of BMI?

```
ggplot(smartcle2, aes(bmi)) +
  geom_histogram(bins = 30, col = "white")
```



2.5.4 How many of the respondents have a BMI below 30?

2.5.5 How many of the respondents who have a BMI < 30 exercised?

```
smartcle2 %>% count(exerany, bmi < 30) %>%
    group_by(exerany) %>%
    mutate(percent = 100*n/sum(n))
# A tibble: 4 x 4
# Groups: exerany [2]
  exerany `bmi < 30`
                         n percent
    <int> <lgl>
                             <dbl>
                     <int>
1
        0 F
                        88
                              42.1
2
        0 T
                       121
                              57.9
3
        1 F
                       165
                              24.0
4
        1 T
                       522
                              76.0
```

2.5.6 Is obesity associated with sex, in these data?

```
smartcle2 %>% count(female, bmi < 30) %>%
    group_by(female) %>%
    mutate(percent = 100*n/sum(n))
# A tibble: 4 x 4
# Groups: female [2]
  female `bmi < 30`</pre>
                         n percent
   <int> <lgl>
                              <dbl>
                     <int>
       0 F
                       105
                               28.2
1
2
       0 T
                       267
                              71.8
3
       1 F
                       148
                              28.2
4
       1 T
                       376
                              71.8
```

2.5.7 Comparing sleephrs summaries by obesity status

Can we compare the sleephrs means, medians and 75th percentiles for respondents whose BMI is below 30 to the respondents whose BMI is not?

2.5.8 The skim function within a pipe

The **skim** function works within pipes and with the other **tidyverse** functions.

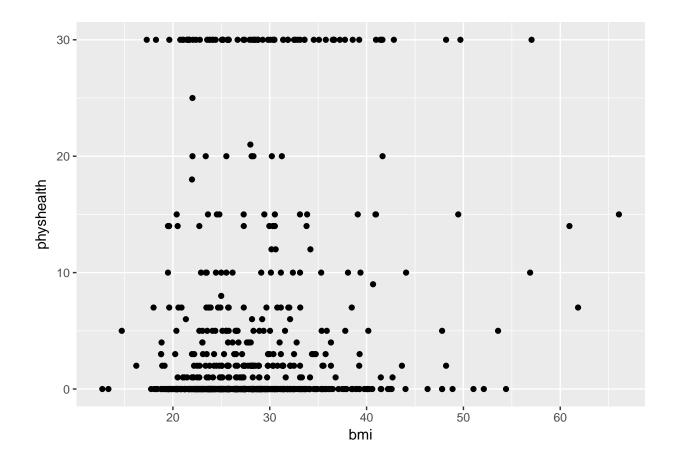
```
smartcle2 %>%
   group_by(exerany) %>%
   skim(bmi, sleephrs)
Skim summary statistics
n obs: 896
n variables: 10
group variables: exerany
Variable type: integer
exerany variable missing complete
                                    n mean sd p0 p25 median p75 p100
      0 sleephrs
                       0
                          209 209 7
                                           1.85 1
                                                            7
                                                                    20
                       0
                              687 687 7.03 1.34 1
      1 sleephrs
                                                            7
                                                                    16
Variable type: numeric
 exerany variable missing complete
                                                         p25 median
                                    n mean
                                              sd
                                                    p0
      0
             bmi
                       0
                              209 209 29.57 7.46 18
                                                       24.11 28.49 33.13
      1
             bmi
                              687 687 27.35 5.84 12.71 23.7
                                                              26.52 29.81
 p100
```

66.06 60.95

2.6 First Modeling Attempt: Can bmi predict physhealth?

We'll start with an effort to predict physhealth using bmi. A natural graph would be a scatterplot.

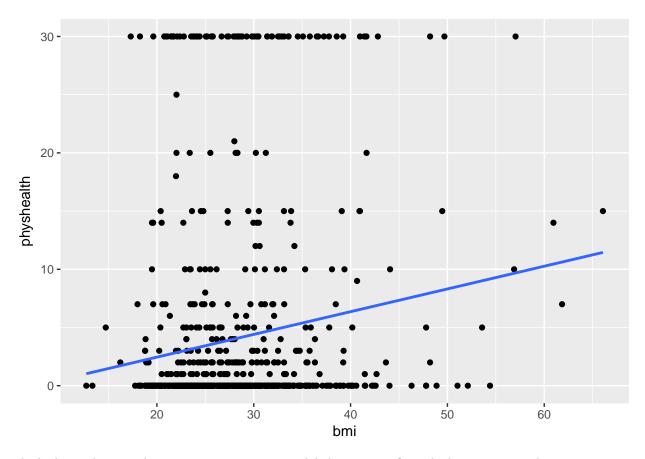
```
ggplot(data = smartcle2, aes(x = bmi, y = physhealth)) +
   geom_point()
```



A good question to ask ourselves here might be: "In what BMI range can we make a reasonable prediction of physhealth?"

Now, we might take the plot above and add a simple linear model ...

```
ggplot(data = smartcle2, aes(x = bmi, y = physhealth)) +
   geom_point() +
   geom_smooth(method = "lm", se = FALSE)
```



which shows the same least squares regression model that we can fit with the ${\tt lm}$ command.

2.6.1 Fitting a Simple Regression Model

```
Call:
lm(formula = physhealth ~ bmi, data = smartcle2)
Residuals:
   Min   1Q Median   3Q   Max
-9.171 -4.057 -3.193 -1.576 28.073
```

Coefficients:

```
Estimate Std. Error t value Pr(>|t|)
(Intercept) -1.45143
                       1.29185 -1.124
bmi
            0.19527
                        0.04521
                                  4.319 1.74e-05 ***
Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' ' 1
Residual standard error: 8.556 on 894 degrees of freedom
Multiple R-squared: 0.02044,
                               Adjusted R-squared: 0.01934
F-statistic: 18.65 on 1 and 894 DF, p-value: 1.742e-05
confint(model_A, level = 0.95)
                 2.5 %
                          97.5 %
(Intercept) -3.9868457 1.0839862
            0.1065409 0.2840068
```

The model coefficients can be obtained by printing the model object, and the summary function provides several useful descriptions of the model's residuals, its statistical significance, and quality of fit.

2.6.2 Model Summary for a Simple (One-Predictor) Regression

The fitted model predicts physhealth with the equation -1.45 + 0.195*bmi, as we can read off from the model coefficients.

Each of the 896 respondents included in the smartcle2 data makes a contribution to this model.

2.6.2.1 Residuals

Suppose Harry is one of the people in that group, and Harry's data is bmi = 20, and physhealth = 3.

- Harry's *observed* value of physhealth is just the value we have in the data for them, in this case, observed physhealth = 3 for Harry.
- Harry's fitted or predicted physhealth value is the result of calculating -1.45 + 0.195bmi for Harry. So, if Harry's BMI was 20, then Harry's predicted physhealth value is -1.45 + (0.19520) = 2.45.
- The residual for Harry is then his observed outcome minus his fitted outcome, so Harry has a residual of 3 2.45 = 0.55.
- Graphically, a residual represents vertical distance between the observed point and the fitted regression line.
- Points above the regression line will have positive residuals, and points below the regression line will have negative residuals. Points on the line have zero residuals.

The residuals are summarized at the top of the summary output for linear model.

- The mean residual will always be zero in an ordinary least squares model, but a five number summary of the residuals is provided by the summary, as is an estimated standard deviation of the residuals (called here the Residual standard error.)
- In the smartcle2 data, the minimum residual was -9.17, so for one subject, the observed value was 9.17 days smaller than the predicted value. This means that the prediction was 9.17 days too large for that subject.
- Similarly, the maximum residual was 28.07 days, so for one subject the prediction was 28.07 days too small. Not a strong performance.
- In a least squares model, the residuals are assumed to follow a Normal distribution, with mean zero, and standard deviation (for the smartcle2 data) of about 8.6 days. Thus, by the definition of a Normal distribution, we'd expect
- about 68% of the residuals to be between -8.6 and +8.6 days,

- about 95% of the residuals to be between -17.2 and +17.2 days,
- about all (99.7%) of the residuals to be between -25.8 and +25.8 days.

2.6.2.2 Coefficients section

The summary for a linear model shows Estimates, Standard Errors, t values and p values for each coefficient fit.

- The Estimates are the point estimates of the intercept and slope of bmi in our model.
- In this case, our estimated slope is 0.195, which implies that if Harry's BMI is 20 and Sally's BMI is 21, we predict that Sally's physhealth will be 0.195 days larger than Harry's.
- The Standard Errors are also provided for each estimate. We can create rough 95% confidence intervals by adding and subtracting two standard errors from each coefficient, or we can get a slightly more accurate answer with the confint function.
- Here, the 95% confidence interval for the slope of bmi is estimated to be (0.11, 0.28). This is a good measure of the uncertainty in the slope that is captured by our model. We are 95% confident in the process of building this interval, but this doesn't mean we're 95% sure that the true slope is actually in that interval.

Also available are a t value (just the Estimate divided by the Standard Error) and the appropriate p value for testing the null hypothesis that the true value of the coefficient is 0 against a two-tailed alternative.

- If a slope coefficient is statistically significantly different from 0, this implies that 0 will not be part of the uncertainty interval obtained through confint.
- If the slope was zero, it would suggest that bmi would add no predictive value to the model. But that's unlikely here.

If the bmi slope coefficient is associated with a small p value, as in the case of our model_A, it suggests that the model including bmi is statistically significantly better at predicting physhealth than the model without bmi.

• Without bmi our model_A would become an *intercept-only* model, in this case, which would predict the mean physhealth for everyone, regardless of any other information.

2.6.2.3 Model Fit Summaries

The summary of a linear model also displays:

- The residual standard error and associated degrees of freedom for the residuals.
- For a simple (one-predictor) least regression like this, the residual degrees of freedom will be the sample size minus 2.
- The multiple R-squared (or coefficient of determination)
- This is interpreted as the proportion of variation in the outcome (physhealth) accounted for by the model, and will always fall between 0 and 1 as a result.
- Our model A accounts for a mere 2% of the variation in physhealth.
- The Adjusted R-squared value "adjusts" for the size of our model in terms of the number of coefficients included in the model.
- The adjusted R-squared will always be less than the Multiple R-squared.
- We still hope to find models with relatively large adjusted R² values.
- In particular, we hope to find models where the adjusted R² isn't substantially less than the Multiple R-squared.
- The adjusted R-squared is usually a better estimate of likely performance of our model in new data than is the Multiple R-squared.
- The adjusted R-squared result is no longer interpretable as a proportion of anything in fact, it can fall below 0.

• We can obtain the adjusted \mathbb{R}^2 from the raw \mathbb{R}^2 , the number of observations N and the number of predictors p included in the model, as follows:

$$R_{adj}^2 = 1 - \frac{(1 - R^2)(N - 1)}{N - p - 1},$$

- The F statistic and p value from a global ANOVA test of the model.
 - Obtaining a statistically significant result here is usually pretty straightforward, since the comparison is between our model, and a model which simply predicts the mean value of the outcome for everyone.
 - In a simple (one-predictor) linear regression like this, the t statistic for the slope is just the square root of the F statistic, and the resulting p values for the slope's t test and for the global F test will be identical.
- To see the complete ANOVA F test for this model, we can run anova(model_A).

```
anova(model_A)
```

Analysis of Variance Table

```
Response: physhealth

Df Sum Sq Mean Sq F value Pr(>F)

bmi 1 1366 1365.5 18.655 1.742e-05 ***

Residuals 894 65441 73.2

---

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

2.6.3 Using the broom package

The broom package has three functions of particular use in a linear regression model:

2.6.3.1 The tidy function

tidy builds a data frame/tibble containing information about the coefficients in the model, their standard errors, t statistics and p values.

```
tidy(model_A)
```

```
term estimate std.error statistic p.value
1 (Intercept) -1.4514298 1.29185199 -1.123526 2.615156e-01
2 bmi 0.1952739 0.04521145 4.319125 1.741859e-05
```

2.6.3.2 The glance function

glance' builds a data frame/tibble containing summary statistics about the model, including

- the (raw) multiple R² and adjusted R²
- sigma which is the residual standard error
- the F statistic, p.value model df and df.residual associated with the global ANOVA test, plus
- several statistics that will be useful in comparing models down the line:
- the model's log likelihood function value, logLik
- the model's Akaike's Information Criterion value, AIC
- the model's Bayesian Information Criterion value, BIC
- and the model's deviance statistic

glance(model_A)

```
r.squared adj.r.squared sigma statistic p.value df logLik
1 0.02044019 0.01934449 8.555737 18.65484 1.741859e-05 2 -3193.723
AIC BIC deviance df.residual
1 6393.446 6407.84 65441.36 894
```

2.6.3.3 The augment function

augment builds a data frame/tibble which adds fitted values, residuals and other diagnostic summaries that describe each observation to the original data used to fit the model, and this includes

- .fitted and .resid, the fitted and residual values, in addition to
- .hat, the leverage value for this observation
- .cooksd, the Cook's distance measure of influence for this observation
- .stdresid, the standardized residual (think of this as a z-score a measure of the residual divided by its associated standard deviation .sigma)
- · and se.fit which will help us generate prediction intervals for the model downstream

Note that each of the new columns begins with . to avoid overwriting any data.

```
head(augment(model_A))
```

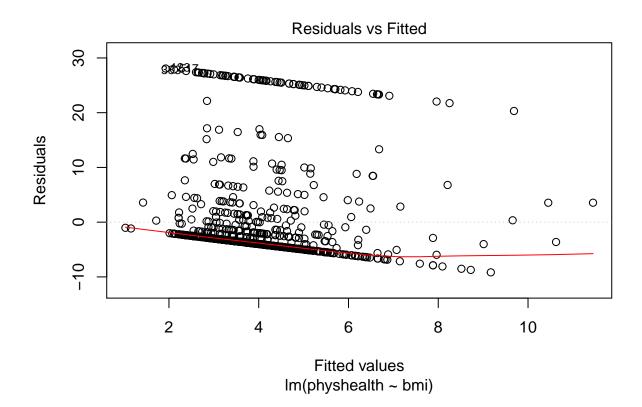
```
physhealth
               bmi
                   .fitted
                              .se.fit
                                                                 .sigma
                                            .resid
                                                          .hat
           0 26.69 3.760430 0.2907252 -3.76043009 0.001154651 8.559600
           0 23.70 3.176561 0.3422908 -3.17656119 0.001600574 8.559865
2
           1 26.92 3.805343 0.2890054 -2.80534308 0.001141030 8.560010
           0 21.66 2.778202 0.4005101 -2.77820248 0.002191352 8.560020
           5 24.09 3.252718 0.3329154 1.74728200 0.001514095 8.560326
5
           4 27.64 3.945940 0.2860087 0.05405972 0.001117490 8.560526
                 .std.resid
       .cooksd
1 1.117852e-04 -0.439775451
2 1.106717e-04 -0.371575999
3 6.147744e-05 -0.328077528
4 1.160381e-04 -0.325074461
5 3.167016e-05 0.204378225
6 2.235722e-08 0.006322069
```

For more on the broom package, you may want to look at this vignette.

2.6.4 How does the model do? (Residuals vs. Fitted Values)

• Remember that the R^2 value was about 2%.

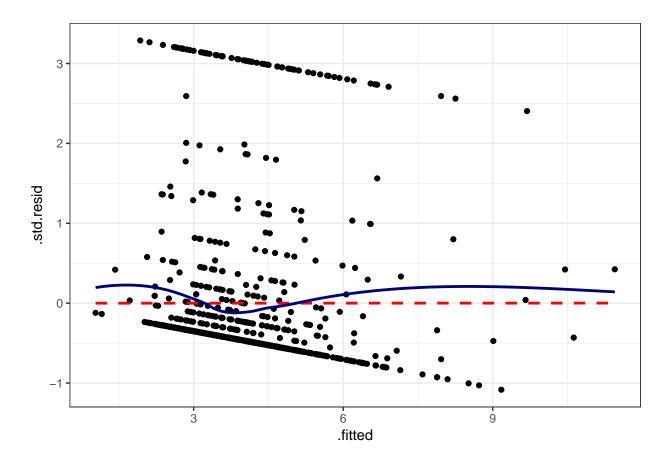
```
plot(model_A, which = 1)
```



This is a plot of residuals vs. fitted values. The goal here is for this plot to look like a random scatter of points, perhaps like a "fuzzy football", and that's **not** what we have. Why?

If you prefer, here's a ggplot2 version of a similar plot, now looking at standardized residuals instead of raw residuals, and adding a loess smooth and a linear fit to the result.

```
ggplot(augment(model_A), aes(x = .fitted, y = .std.resid)) +
    geom_point() +
    geom_smooth(method = "lm", se = FALSE, col = "red", linetype = "dashed") +
    geom_smooth(method = "loess", se = FALSE, col = "navy") +
    theme_bw()
```



The problem we're having here becomes, I think, a little more obvious if we look at what we're predicting. Does physhealth look like a good candidate for a linear model?

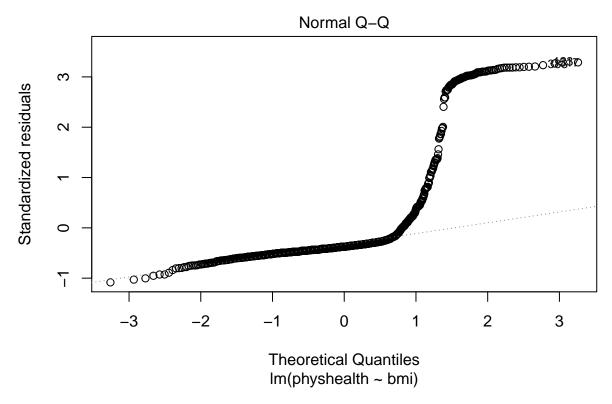
```
ggplot(smartcle2, aes(x = physhealth)) +
geom_histogram(bins = 30, fill = "dodgerblue", color = "royalblue")
```



No matter what model we fit, if we are predicting physhealth, and most of the data are values of 0 and 30, we have limited variation in our outcome, and so our linear model will be somewhat questionable just on that basis.

A normal Q-Q plot of the standardized residuals for our model_A shows this problem, too.

plot(model_A, which = 2)



We're going to need a method to deal with this sort of outcome, that has both a floor and a ceiling. We'll get there eventually, but linear regression alone doesn't look promising.

All right, so that didn't go anywhere great. Let's try again, with a new outcome.

2.7 A New Small Study: Predicting BMI

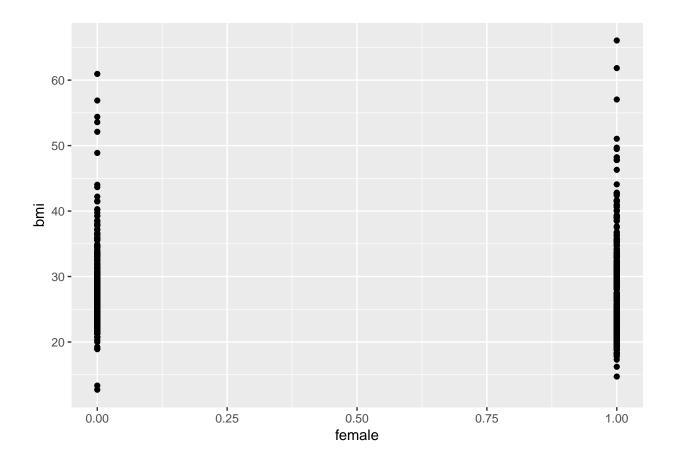
We'll begin by investigating the problem of predicting bmi, at first with just three regression inputs: sex, exerany and sleephrs, in our new smartcle2 data set.

- The outcome of interest is bmi.
- Inputs to the regression model are:
 - female = 1 if the subject is female, and 0 if they are male
 - exerany = 1 if the subject exercised in the past 30 days, and 0 if they didn't
 - sleephrs = hours slept in a typical 24-hour period (treated as quantitative)

2.7.1 Does female predict bmi well?

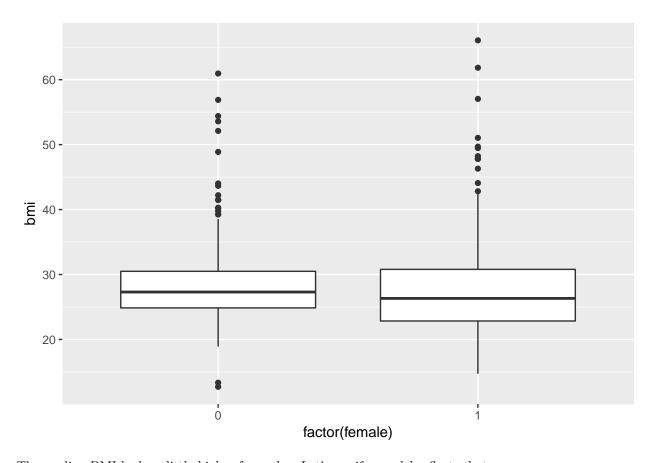
2.7.1.1 Graphical Assessment

```
ggplot(smartcle2, aes(x = female, y = bmi)) +
   geom_point()
```



Not so helpful. We should probably specify that female is a factor, and try another plotting approach.

```
ggplot(smartcle2, aes(x = factor(female), y = bmi)) +
   geom_boxplot()
```



The median BMI looks a little higher for males. Let's see if a model reflects that.

2.8 c2_m1: A simple t-test model

Coefficients:

Min 1Q Median 3Q Max -15.650 -4.129 -1.080 2.727 38.546

Residuals:

```
2.5 % 97.5 % (Intercept) 27.717372 29.00262801 female -1.686052 -0.00539878
```

The model suggests, based on these 896 subjects, that

- our best prediction for males is $BMI = 28.36 \text{ kg/m}^2$, and
- our best prediction for females is BMI = $28.36 0.85 = 27.51 \text{ kg/m}^2$.
- the mean difference between females and males is -0.85 kg/m^2 in BMI
- \bullet a 95% confidence (uncertainty) interval for that mean female male difference in BMI ranges from -1.69 to -0.01
- the model accounts for 0.4% of the variation in BMI, so that knowing the respondent's sex does very little to reduce the size of the prediction errors as compared to an intercept only model that would predict the overall mean (regardless of sex) for all subjects.
- the model makes some enormous errors, with one subject being predicted to have a BMI 38 points lower than his/her actual BMI.

Note that this simple regression model just gives us the t-test.

t.test(bmi ~ female, var.equal = TRUE, data = smartcle2)

```
Two Sample t-test

data: bmi by female

t = 1.9752, df = 894, p-value = 0.04855

alternative hypothesis: true difference in means is not equal to 0

95 percent confidence interval:
0.00539878 1.68605160

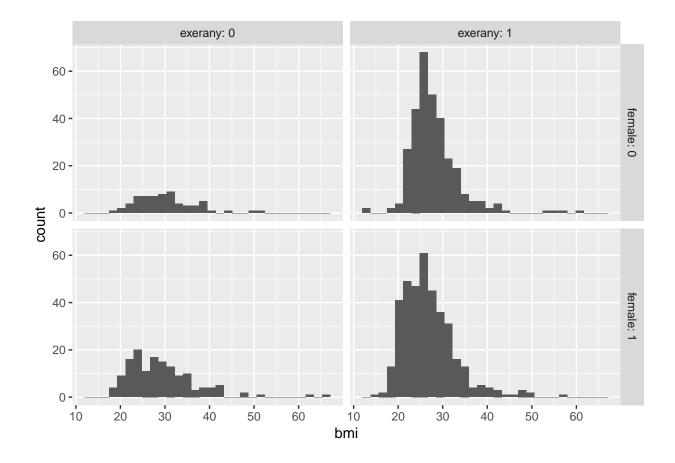
sample estimates:
mean in group 0 mean in group 1
28.36000 27.51427
```

2.9 c2_m2: Adding another predictor (two-way ANOVA without interaction)

When we add in the information about exerany to our original model, we might first picture the data. We could look at separate histograms,

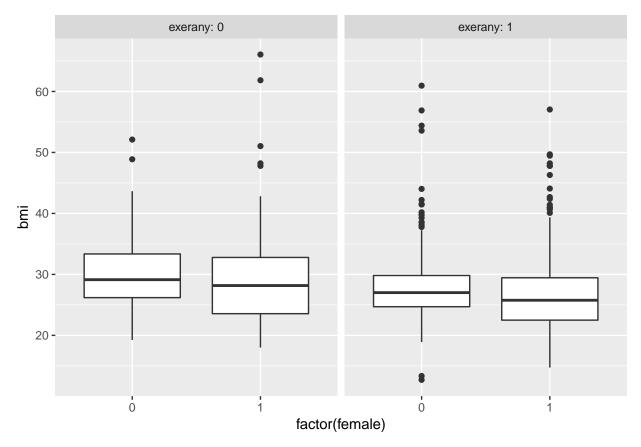
```
ggplot(smartcle2, aes(x = bmi)) +
   geom_histogram(bins = 30) +
   facet_grid(female ~ exerany, labeller = label_both)
```



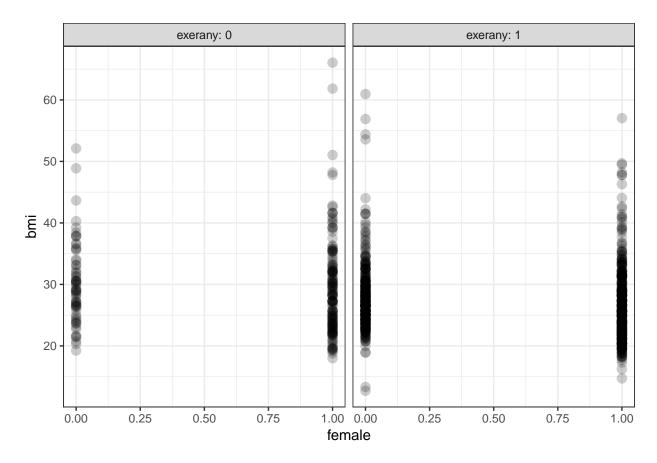


or maybe boxplots?

```
ggplot(smartcle2, aes(x = factor(female), y = bmi)) +
    geom_boxplot() +
   facet_wrap(~ exerany, labeller = label_both)
```



```
ggplot(smartcle2, aes(x = female, y = bmi))+
  geom_point(size = 3, alpha = 0.2) +
  theme_bw() +
  facet_wrap(~ exerany, labeller = label_both)
```



OK. Let's try fitting a model.

```
c2_m2 <- lm(bmi ~ female + exerany, data = smartcle2)</pre>
c2_m2
```

Call:

lm(formula = bmi ~ female + exerany, data = smartcle2)

Coefficients:

(Intercept) female exerany 30.334 -1.095 -2.384

This new model predicts only four predicted values:

- bmi = 30.334 if the subject is male and did not exercise (so female = 0 and exerany = 0)
- bmi = 30.334 1.095 = 29.239 if the subject is female and did not exercise (female = 1 and exerany = 0)
- bmi = 30.334 2.384 = 27.950 if the subject is male and exercised (so female = 0 and exerany = 1), and, finally
- bmi = 30.334 1.095 2.384 = 26.855 if the subject is female and exercised (so both female and exerany = 1).

For those who did not exercise, the model is:

• bmi = 30.334 - 1.095 female

and for those who did exercise, the model is:

• bmi = 27.95 - 1.095 female

Only the intercept of the bmi-female model changes depending on exerany.

```
summary(c2_m2)
lm(formula = bmi ~ female + exerany, data = smartcle2)
Residuals:
            1Q Median
   Min
                            3Q
                                   Max
-15.240 -4.091 -1.095
                         2.602 36.822
Coefficients:
           Estimate Std. Error t value Pr(>|t|)
(Intercept) 30.3335
                        0.5231
                                 57.99 < 2e-16 ***
            -1.0952
                        0.4262
                                -2.57
                                        0.0103 *
female
exerany
            -2.3836
                        0.4965
                                -4.80 1.86e-06 ***
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
Residual standard error: 6.239 on 893 degrees of freedom
                              Adjusted R-squared: 0.02722
Multiple R-squared: 0.02939,
F-statistic: 13.52 on 2 and 893 DF, p-value: 1.641e-06
confint(c2 m2)
```

```
2.5 % 97.5 % (Intercept) 29.306846 31.3602182 female -1.931629 -0.2588299 exerany -3.358156 -1.4090777
```

The slopes of both female and exerany have confidence intervals that are completely below zero, indicating that both female sex and exerany appear to be associated with reductions in bmi.

The R² value suggests that just under 3% of the variation in bmi is accounted for by this ANOVA model.

In fact, this regression (on two binary indicator variables) is simply a two-way ANOVA model without an interaction term.

```
anova(c2_m2)
```

Analysis of Variance Table

```
Response: bmi

Df Sum Sq Mean Sq F value Pr(>F)

female 1 156 155.61 3.9977 0.04586 *

exerany 1 897 896.93 23.0435 1.856e-06 ***

Residuals 893 34759 38.92

---

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

2.10 c2_m3: Adding the interaction term (Two-way ANOVA with interaction)

Suppose we want to let the effect of female vary depending on the exerany status. Then we need to incorporate an interaction term in our model.

```
c2_m3 <- lm(bmi ~ female * exerany, data = smartcle2)</pre>
c2_m3
```

Call:

lm(formula = bmi ~ female * exerany, data = smartcle2)

Coefficients:

(Intercept) female exerany female:exerany -0.8104 -2.1450-0.359230.1359

So, for example, for a male who exercises, this model predicts

• bmi = 30.136 - 0.810(0) - 2.145(1) - 0.359(0)(1) = 30.136 - 2.145 = 27.991

And for a female who exercises, the model predicts

•
$$bmi = 30.136 - 0.810$$
 (1) - 2.145 (1) - 0.359 (1)(1) = 30.136 - 0.810 - 2.145 - 0.359 = 26.822

For those who did not exercise, the model is:

• bmi = 30.136 - 0.81 female

But for those who did exercise, the model is:

- bmi = (30.136 2.145) + (-0.810 + (-0.359)) female, or ",
- $\bullet \ \operatorname{bmi} = 27.991 1.169 \ \operatorname{female}$

Now, both the slope and the intercept of the bmi-female model change depending on exerany.

```
summary(c2_m3)
```

Call:

lm(formula = bmi ~ female * exerany, data = smartcle2)

Residuals:

```
1Q Median
                          3Q
   Min
                                Max
-15.281 -4.101 -1.061
                       2.566 36.734
```

Coefficients:

```
Estimate Std. Error t value Pr(>|t|)
(Intercept)
             30.1359 0.7802 38.624
                                          <2e-16 ***
female
              -0.8104
                          0.9367 - 0.865
                                          0.3872
              -2.1450
                          0.8575 - 2.501
                                          0.0125 *
exerany
female:exerany -0.3592
                                          0.7328
                          1.0520 -0.341
```

Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1

Residual standard error: 6.242 on 892 degrees of freedom Multiple R-squared: 0.02952, Adjusted R-squared: 0.02625 F-statistic: 9.044 on 3 and 892 DF, p-value: 6.669e-06

confint(c2 m3)

```
2.5 %
                            97.5 %
              28.604610 31.6672650
(Intercept)
female
              -2.648893 1.0280526
exerany
              -3.827886 -0.4620407
female:exerany -2.423994 1.7055248
```

In fact, this regression (on two binary indicator variables and a product term) is simply a two-way ANOVA model with an interaction term.

```
anova(c2_m3)
```

Analysis of Variance Table

```
Response: bmi
               Df Sum Sq Mean Sq F value
                                            Pr(>F)
female
                     156 155.61 3.9938
                                           0.04597 *
exerany
                     897
                          896.93 23.0207 1.878e-06 ***
female: exerany
                       5
                            4.54
                                 0.1166
                                           0.73283
Residuals
              892
                  34754
                           38.96
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
```

The interaction term doesn't change very much here. Its uncertainty interval includes zero, and the overall model still accounts for just under 3% of the variation in bmi.

2.11 c2_m4: Using female and sleephrs in a model for bmi

```
ggplot(smartcle2, aes(x = sleephrs, y = bmi, color = factor(female))) +
    geom_point() +
    guides(col = FALSE) +
    geom_smooth(method = "lm", se = FALSE) +
    facet_wrap(~ female, labeller = label_both)
```



Does the difference in slopes of bmi and sleephrs for males and females appear to be substantial and important?

```
c2_m4 <- lm(bmi ~ female * sleephrs, data = smartcle2)
summary(c2_m4)</pre>
```

Call:

lm(formula = bmi ~ female * sleephrs, data = smartcle2)

Residuals:

```
Min 1Q Median 3Q Max
-15.498 -4.179 -1.035 2.830 38.204
```

Coefficients:

```
Estimate Std. Error t value Pr(>|t|)
(Intercept)
                27.2661
                            1.6320 16.707
                                             <2e-16 ***
female
                 2.5263
                            2.0975
                                    1.204
                                              0.229
                 0.1569
                            0.2294
                                     0.684
                                              0.494
sleephrs
female:sleephrs
               -0.4797
                            0.2931 - 1.636
                                              0.102
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
```

Residual standard error: 6.31 on 892 degrees of freedom Multiple R-squared: 0.008341, Adjusted R-squared: 0.005006

F-statistic: 2.501 on 3 and 892 DF, p-value: 0.05818

Does it seem as though the addition of sleephrs has improved our model substantially over a model with female alone (which, you recall, was c2_m1)?

Since the c2_m4 model contains the c2_m1 model's predictors as a subset and the outcome is the same for each model, we consider the models *nested* and have some extra tools available to compare them.

• I might start by looking at the basic summaries for each model.

```
glance(c2_m4)
```

```
r.squared adj.r.squared sigma statistic p.value df logLik
1 0.008341404 0.005006229 6.309685 2.50104 0.05818038 4 -2919.873
    AIC BIC deviance df.residual
1 5849.747 5873.736 35512.42 892

glance(c2_m1)
```

```
r.squared adj.r.squared sigma statistic p.value df logLik
1 0.004345169 0.003231461 6.31531 3.901534 0.04854928 2 -2921.675
AIC BIC deviance df.residual
1 5849.35 5863.744 35655.53 894
```

- The R² is twice as large for the model with sleephrs, but still very tiny.
- The p value for the global ANOVA test is actually less significant in c2_m4 than in c2_m1.
- Smaller AIC and smaller BIC statistics are more desirable. Here, there's little to choose from, but c2_m1 is a little better on each standard.
- We might also consider a significance test by looking at an ANOVA model comparison. This is only
 appropriate because c2_m1 is nested in c2_m4.

```
anova(c2_m4, c2_m1)
```

Analysis of Variance Table

```
Model 1: bmi ~ female * sleephrs

Model 2: bmi ~ female

Res.Df RSS Df Sum of Sq F Pr(>F)

1 892 35512

2 894 35656 -2 -143.11 1.7973 0.1663
```

The addition of the sleephrs term picked up 143 in the sum of squares column, at a cost of two degrees of freedom, yielding a p value of 0.166, suggesting that this isn't a significant improvement over the model that just did a t-test on female.

2.12 c2_m5: What if we add more variables?

We can boost our R² a bit, to over 5%, by adding in two new variables, related to whether or not the subject (in the past 30 days) used the internet, and on how many days the subject drank alcoholic beverages.

Call:

```
lm(formula = bmi ~ female + exerany + sleephrs + internet30 +
alcdays, data = smartcle2)
```

Residuals:

```
Min 1Q Median 3Q Max
-16.147 -3.997 -0.856 2.487 35.965
```

Coefficients:

```
Estimate Std. Error t value Pr(>|t|)
(Intercept) 30.84066 1.18458 26.035 < 2e-16 ***
female
           -1.28801
                       0.42805 - 3.009
                                        0.0027 **
           -2.42161
                      0.49853
                               -4.858 1.40e-06 ***
exerany
sleephrs
           -0.14118
                       0.13988 -1.009
                                        0.3131
internet30 1.38916
                       0.54252
                                2.561
                                        0.0106 *
alcdays
           -0.10460
                       0.02595 -4.030 6.04e-05 ***
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
```

Residual standard error: 6.174 on 890 degrees of freedom Multiple R-squared: 0.05258, Adjusted R-squared: 0.04726 F-statistic: 9.879 on 5 and 890 DF, p-value: 3.304e-09

1. Here's the ANOVA for this model. What can we study with this?

```
anova(c2_m5)
```

Analysis of Variance Table

```
Response: bmi
```

```
Df Sum Sq Mean Sq F value Pr(>F)

female 1 156 155.61 4.0818 0.04365 *

exerany 1 897 896.93 23.5283 1.453e-06 ***

sleephrs 1 33 32.90 0.8631 0.35313
```

```
1
                 178 178.33 4.6779
internet30
                 619 619.26 16.2443 6.044e-05 ***
alcdays
            1
                       38.12
Residuals 890 33928
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
  2. Consider the revised output below. Now what can we study?
anova(lm(bmi ~ exerany + internet30 + alcdays + female + sleephrs,
        data = smartcle2))
Analysis of Variance Table
Response: bmi
           Df Sum Sq Mean Sq F value
                 795 795.46 20.8664 5.618e-06 ***
exerany
                 212 211.95 5.5599 0.0185925 *
internet30
            1
                 486 486.03 12.7496 0.0003752 ***
alcdays
            1
female
                 351 350.75 9.2010 0.0024891 **
                       38.83 1.0186 0.3131176
sleephrs
                  39
            1
Residuals 890 33928
                       38.12
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
  3. What does the output below let us conclude?
anova(lm(bmi ~ exerany + internet30 + alcdays + female + sleephrs,
        data = smartcle2),
     lm(bmi ~ exerany + female + alcdays,
        data = smartcle2))
Analysis of Variance Table
Model 1: bmi ~ exerany + internet30 + alcdays + female + sleephrs
Model 2: bmi ~ exerany + female + alcdays
                               F Pr(>F)
 Res.Df RSS Df Sum of Sq
    890 33928
    892 34221 -2
                    -293.2 3.8456 0.02173 *
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
  4. What does it mean for the models to be "nested"?
```

2.13 c2_m6: Would adding self-reported health help?

And we can do even a bit better than that by adding in a multi-categorical measure: self-reported general health.

```
Call:
lm(formula = bmi ~ female + exerany + sleephrs + internet30 +
    alcdays + genhealth, data = smartcle2)
```

```
Residuals:
```

```
Min 1Q Median 3Q Max
-16.331 -3.813 -0.838 2.679 34.166
```

Coefficients:

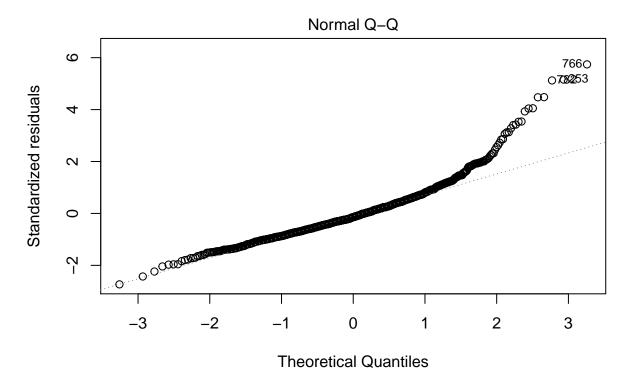
```
Estimate Std. Error t value Pr(>|t|)
(Intercept)
                                1.31121 20.206 < 2e-16 ***
                    26.49498
female
                    -0.85520
                                0.41969 -2.038 0.041879 *
                                0.50541 -3.205 0.001400 **
exerany
                    -1.61968
sleephrs
                    -0.12719
                                0.13613 -0.934 0.350368
internet30
                     2.02498
                                0.53898
                                          3.757 0.000183 ***
                                0.02537
                                         -3.324 0.000925 ***
alcdays
                    -0.08431
genhealth2_VeryGood 2.10537
                                0.59408
                                         3.544 0.000415 ***
genhealth3_Good
                     4.08245
                                0.60739
                                          6.721 3.22e-11 ***
                                0.80178
                                          6.226 7.37e-10 ***
genhealth4_Fair
                     4.99213
genhealth5_Poor
                     3.11025
                                1.12614
                                          2.762 0.005866 **
```

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

Residual standard error: 5.993 on 886 degrees of freedom Multiple R-squared: 0.1115, Adjusted R-squared: 0.1024 F-statistic: 12.35 on 9 and 886 DF, p-value: < 2.2e-16

1. If Harry and Marty have the same values of female, exerany, sleephrs, internet30 and alcdays, but Harry rates his health as Good, and Marty rates his as Fair, then what is the difference in the predictions? Who is predicted to have a larger BMI, and by how much?

2. What does this normal probability plot of the residuals suggest?



Im(bmi ~ female + exerany + sleephrs + internet30 + alcdays + genhealth)

2.14 c2_m7: What if we added days of work missed?

Call:

```
lm(formula = bmi ~ female + exerany + sleephrs + internet30 +
    alcdays + genhealth + physhealth + menthealth, data = smartcle2)
```

Residuals:

```
Min 1Q Median 3Q Max
-16.060 -3.804 -0.890 2.794 33.972
```

Coefficients:

	Estimate S	td. Error	t value	Pr(> t)	
(Intercept)	25.88208	1.31854	19.629	< 2e-16	***
female	-0.96435	0.41908	-2.301	0.021616	*
exerany	-1.43171	0.50635	-2.828	0.004797	**
sleephrs	-0.08033	0.13624	-0.590	0.555583	
internet30	2.00267	0.53759	3.725	0.000207	***
alcdays	-0.07997	0.02528	-3.163	0.001614	**

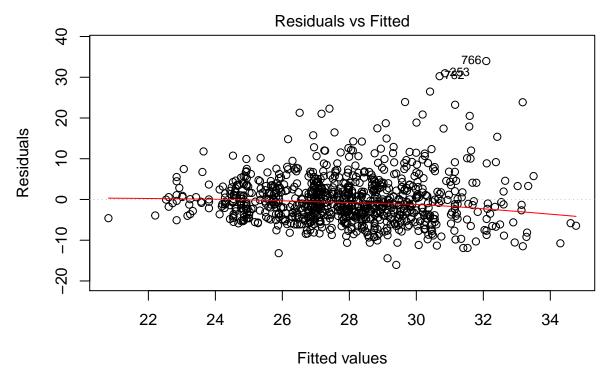
```
3.537 0.000425 ***
genhealth2_VeryGood 2.09533
                                 0.59238
genhealth3_Good
                     3.90949
                                 0.60788
                                           6.431 2.07e-10 ***
genhealth4_Fair
                     4.27152
                                 0.83986
                                           5.086 4.47e-07 ***
genhealth5_Poor
                                           0.958 0.338361
                     1.26021
                                 1.31556
physhealth
                     0.06088
                                 0.03005
                                           2.026 0.043064 *
menthealth
                     0.06636
                                 0.03177
                                           2.089 0.037021 *
```

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

Residual standard error: 5.964 on 884 degrees of freedom Multiple R-squared: 0.1219, Adjusted R-squared: 0.111 F-statistic: 11.16 on 11 and 884 DF, p-value: < 2.2e-16

1. How do the assumptions behind this model look?

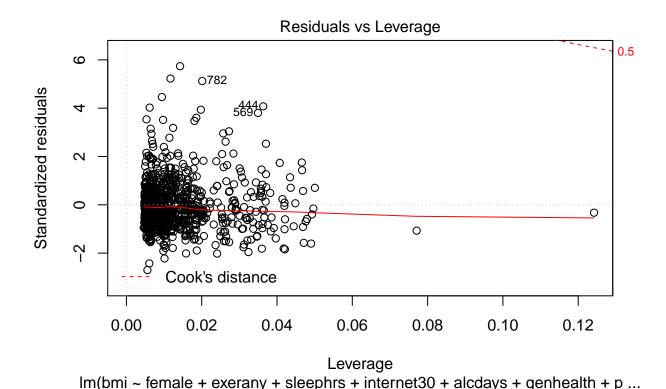
```
plot(c2_m7, which = 1)
```



lm(bmi ~ female + exerany + sleephrs + internet30 + alcdays + genhealth + p ...

2. What can we conclude from the plot below?

```
plot(c2_m7, which = 5)
```



2.15 (DRAFT material) How might we validate this model?

Here's some early code for that issue, which is built on some material by David Robinson at https://rpubs.com/dgrtwo/cv-modelr

This bit of code performs what is called 10-crossfold separation. In words, this approach splits the 896 observations in our data into 10 exclusive partitions of about 90% into a training sample, and the remaining 10% in a test sample. The next part of the code maps a modeling step to the training data, and then fits the resulting model on the test data using the broom package's augment function.

I've selected the variables in this case so that the model we'll fit is the $m2_c7$ model we've been looking at, although there are several ways to accomplish this.

```
# A tibble: 896 x 10
         bmi female exerany sleephrs internet30 alcdays genhealth
  .id
  <chr> <dbl> <int>
                     <int>
                             <int>
                                      <int>
                                              <int> <fct>
        24.1
1 01
                 0
                        1
                                7
                                                  2 1_Excellent
                                          1
 2 01
        36.4
                 0
                        1
                                8
                                          1
                                                  0 4 Fair
3 01
        32.1
                 1
                        0
                                4
                                          1
                                                  5 2 VeryGood
4 01
        27.3
                 0
                       1
                                8
                                          1
                                                  0 1 Excellent
        28.0
                 0
                                 7
                                                  4 2_VeryGood
5 01
                        1
                                          1
6 01
        22.5
                 1
                        1
                                 7
                                          1
                                                  3 2_VeryGood
        26.3
                0
                                 7
                                                  1 1_Excellent
7 01
                       1
                                          1
8 01
        22.4
                 0
                       1
                                 8
                                          1
                                                  4 1_Excellent
                        0
                                 6
                                                  0 3_Good
9 01
        19.3
                 1
                                          1
10 01
        24.2
                 1
                        0
                                 6
                                          0
                                                  0 3_Good
# ... with 886 more rows, and 2 more variables: .fitted <dbl>, .se.fit
   <dbl>
```

The results are a set of predictions based on the splits into training and test groups (remember there are 10 of them, indexed by .id) that describe the complete set of 896 respondents again.

What this lets us now do is calculate the root Mean Squared Prediction Error (RMSE) and Mean Absolute Prediction Error (MAE) for this model (the c2_m7 model) across these observations, and also to compare that error to a model that simply predicts the mean bmi across all patients (the intercept only model.) In practice, we could consider two distinct models in doing this work.

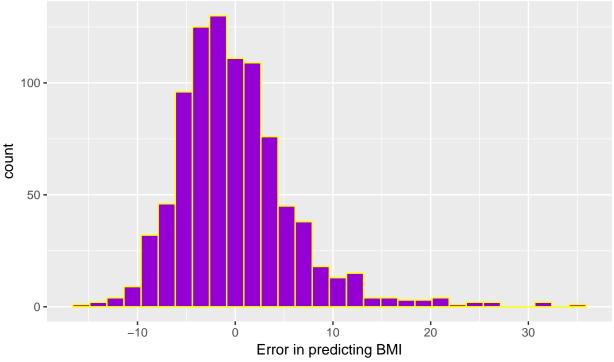
Another thing we could do with this tibble of predictions we have created is to graph the size of the prediction errors (observed bmi minus predicted values in .fitted) that our modeling approach makes.

```
predictions %>%
  mutate(errors = bmi - .fitted) %>%
  ggplot(., aes(x = errors)) +
  geom_histogram(bins = 30, fill = "darkviolet", col = "yellow") +
  labs(title = "Cross-Validated Errors in Prediction of BMI",
      subtitle = "Using a model (`c2_m7`) including 6 regression inputs",
      caption = "SMART BRFSS 2016 data for Cleveland-Elyria MMSA, n = 896",
      x = "Error in predicting BMI")
```

2.16. COMING SOON ... 67

Cross-Validated Errors in Prediction of BMI

Using a model (`c2_m7`) including 6 regression inputs



SMART BRFSS 2016 data for Cleveland-Elyria MMSA, n = 896

2.16 Coming Soon ...

- 1. Would stepwise regression help us build a better model for bmi?
 - Is there a better approach for variable selection? What's this I hear about "best subsets", for example?
- 2. How should we think about potential transformations of these predictors?
 - What's a Spearman rho-squared plot, and how might it help us decide how to spend degrees of freedom on non-linear terms better?
- 3. How do we deal with missing data in fitting and evaluating a linear regression model if we don't actually want to drop all of the incomplete cases?
- 4. How can we use the ols tool in the rms package to fit regression models?
- 5. How can we use the tools in the arm package to fit and evaluate regression models?

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