Clinical Data Analysis

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Contents

Chapter 1

Prerequisites

This is a *sample* book written in **Markdown**. You can use anything that Pandoc's Markdown supports, e.g., a math equation $a^2 + b^2 = c^2$.

The **bookdown** package can be installed from CRAN or Github:

```
install.packages("bookdown")
# or the development version
# devtools::install_github("rstudio/bookdown")
```

Remember each Rmd file contains one and only one chapter, and a chapter is defined by the first-level heading `#`.

To compile this example to PDF, you need XeLaTeX. You are recommended to install TinyTeX (which includes XeLaTeX): https://yihui.org/tinytex/.

Chapter 2

Introduction

You can label chapter and section titles using `{#label}` after them, e.g., we can reference Chapter 2. If you do not manually label them, there will be automatic labels anyway, e.g., Chapter 4.

Figures and tables with captions will be placed in `figure` and `table` environments, respectively.

```
par(mar = c(4, 4, .1, .1))
plot(pressure, type = 'b', pch = 19)
```

Reference a figure by its code chunk label with the `fig:` prefix, e.g., see Figure 2.1. Similarly, you can reference tables generated from `knitr::kable()`, e.g., see Table 2.1.

```
knitr::kable(
  head(iris, 20), caption = 'Here is a nice table!',
  booktabs = TRUE
)
```

You can write citations, too. For example, we are using the **bookdown** package (Xie, 2020) in this sample book, which was built on top of R Markdown and **knitr** (Walker and Shostak, 2010).

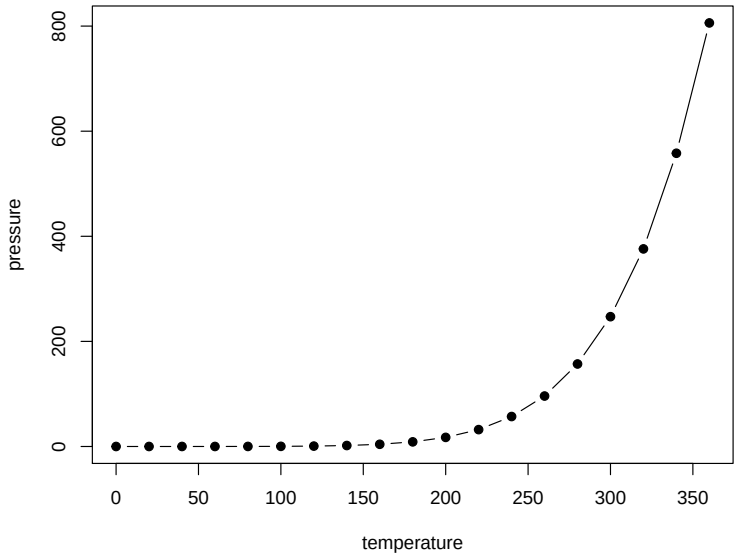

Figure 2.1: Here is a nice figure!

Table 2.1: Here is a nice table!

Sepal.Length	Sepal.Width	Petal.Length	Petal.Width	Species
5.1	3.5	1.4	0.2	setosa
4.9	3.0	1.4	0.2	setosa
4.7	3.2	1.3	0.2	setosa
4.6	3.1	1.5	0.2	setosa
5.0	3.6	1.4	0.2	setosa
5.4	3.9	1.7	0.4	setosa
4.6	3.4	1.4	0.3	setosa
5.0	3.4	1.5	0.2	setosa
4.4	2.9	1.4	0.2	setosa
4.9	3.1	1.5	0.1	setosa
5.4	3.7	1.5	0.2	setosa
4.8	3.4	1.6	0.2	setosa
4.8	3.0	1.4	0.1	setosa
4.3	3.0	1.1	0.1	setosa
5.8	4.0	1.2	0.2	setosa
5.7	4.4	1.5	0.4	setosa
5.4	3.9	1.3	0.4	setosa
5.1	3.5	1.4	0.3	setosa
5.7	3.8	1.7	0.3	setosa
5.1	3.8	1.5	0.3	setosa

Chapter 3

Literature

Here is a review of existing methods.

Chapter 4

Methods

We describe our methods in this chapter.

Chapter 5

Applications

Some *significant* applications are demonstrated in this chapter.

5.1 Example one

5.2 Example two

Chapter 6

Final Words

We have finished a nice book.

Chapter 7

The Binomial Test

7.1 Overview

The **binomial test** is used to make inferences about a proportion or response rate based on a series of independent observations, each resulting in one of two possible mutually exclusive outcomes, such as:

```
+ response to treatment vs. no response

+ cure or no cure

+ survival or death

+ event vs non-event (in general)
```

The total number of *events* in n observations, X, follows the binomial probability distribution. Intuitively, the sample proportion, X/n, would be a good estimate of the unknown population proportion, p. Statistically, it is the best estimate.

You want to determine whether the population proportion, p, differs from a hypothesized value, p_0. If the unknown proportion, p, equals p_0, then the estimated proportion, X/n, should be close to p_0, i.e., X should be close to n * p_0. When p differs from p_0, X might be much larger or smaller than n * p_0.

SAS function, **probbnml()** can be used to determine X_L and X_U (lower limit and upper limit)

7.2 Normal Approximation

For larger values of n and non-extreme values of p, a binomial response, X, can be approximated by a normal distribution with mean n * p and variance n * p * (1-p). This approximation improves as n gets larger or as p gets closer to 0.5

7.3 A proc freq example

```
data acr20;
    input patient $ avalc $ @@;
    cards;
    1 Yes 2 No
    3 Yes 4 No
    5 Yes 6 Yes
    7 No  8 Yes
    9 No  10 No
    11 Yes 12 No
    13 Yes 14 No
    15 Yes 16 No
    17 No  18 Yes
    19 Yes 20 No
    21 Yes 22 Yes
    23 No 24 Yes
    25 Yes
    ;
run;

data acr20a;
    set acr20;
    avalc=ifc(avalc="Yes", "1Yes", "2No");
run;

proc freq data=acr20a;
    tables avalc / binomialc (p = 0.4) alpha=0.05;
    exact binomial;
    title1 "Binomial Test";
run;
```

7.3.1 A real example from trial

TEFHAQ02S2: Number of Subjects Achieving a ≥0.35 Improvement from Baseline in HAQ-DI Scores by Visit from Week 52 Through Week 100; Full Analysis Set 1, Among the Subjects with HAQ-DI Score ≥0.35 at Baseline

	Active Drug		
	Placebo → 100 mg q4w	100 mg q8w	100 mg q4w
Analysis set: Full Analysis Set 1 Among the Subjects with HAQ-DI Score ≥0.35 at Baseline	236	228	228
Week 52[a]			
Subjects with HAQ-DI response	112 (47.5%)	131 (57.5%)	134 (58.8%)
95% CI of response rate[b]	(40.9, 54.0)	(50.8, 64.1)	(52.2, 65.4)
Week 68[a]			
Subjects with HAQ-DI response	123 (52.1%)	137 (60.1%)	143 (62.7%)
95% CI of response rate[b]	(45.5, 58.7)	(53.5, 66.7)	(56.2, 69.2)
Week 76[a]			
Subjects with HAQ-DI response	127 (53.8%)	141 (61.8%)	134 (58.8%)
95% CI of response rate[b]	(47.2, 60.4)	(55.3, 68.4)	(52.2, 65.4)
Week 84[a]			
Subjects with HAQ-DI response	123 (52.1%)	137 (60.1%)	133 (58.3%)
95% CI of response rate[b]	(45.5, 58.7)	(53.5, 66.7)	(51.7, 65.0)
Week 100[a]			
Subjects with HAQ-DI response	131 (55.5%)	145 (63.6%)	143 (62.7%)
95% CI of response rate[b]	(49.0, 62.1)	(57.1, 70.1)	(56.2, 69.2)

[a] Subjects with data missing were considered non-responders.
[b] The confidence intervals for response rates were based on Wald statistic.

7.3.1.1 proc freq to calculate Wald CI

```
data resp;
    input avisitn avisit $ trt01pn avalc $ count;
    cards;
    20052 Week_52 1 N 124
    20052 Week_52 1 Y 112
    20052 Week_52 2 N 97
    20052 Week_52 2 Y 131
    20052 Week_52 3 N 94
    20052 Week_52 3 Y 134
    20068 Week_68 1 N 113
```

```
    20068 Week_68 1 Y 123
    20068 Week_68 2 N 91
    20068 Week_68 2 Y 137
    20068 Week_68 3 N 85
    20068 Week_68 3 Y 143
    ;
run;

proc sort data=resp;
    by avisitn avisit trt01pn;
run;

ods output BinomialCLs=bincl;
proc freq data=resp;
    by avisitn avisit trt01pn;
    table avalc/binomial(level = "Y" CL=WALD(CORRECT));
    weight count;
run;

data resp2;
    set bincl;
    if proportion not in (0,.) then percent = round(proportion * 100, .1);
    if lowercl not in (0,.) then lowercl = round(lowercl * 100, .1);
    else lowercl=0;
    if uppercl not in (0,.) then uppercl = round(uppercl * 100, .1);
    else uppercl=0;
run;
```

SAS doc

Bibliography

Walker, G. A. and Shostak, J. (2010). *Common Statistical Methods for Clinical Research with SAS Examples*. SAS Institute Inc., Cary, NC, 3nd edition. ISBN 978-1-60764-228-2.

Xie, Y. (2020). *bookdown: Authoring Books and Technical Documents with R Markdown*. R package version 0.21.