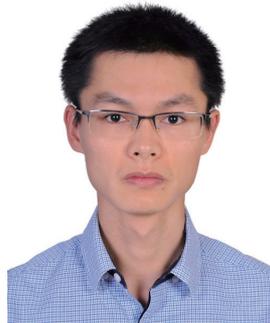


Univariate description and bivariate statistical inference: the first step delving into data

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Author's introduction: Zhongheng Zhang, MMed. Department of Critical Care Medicine, Jinhua Municipal Central Hospital, Jinhua Hospital of Zhejiang University. Dr. Zhongheng Zhang is a fellow physician of the Jinhua Municipal Central Hospital. He graduated from School of Medicine, Zhejiang University in 2009, receiving Master Degree. He has published more than 35 academic papers (science citation indexed) that have been cited for over 200 times. He has been appointed as reviewer for 10 journals, including *Journal of Cardiovascular Medicine*, *Hemodialysis International*, *Journal of Translational Medicine*, *Critical Care*, *International Journal of Clinical Practice*, *Journal of Critical Care*. His major research interests include hemodynamic monitoring in sepsis and septic shock, delirium, and outcome study for critically ill patients. He is experienced in data management and statistical analysis by using R and STATA, big data exploration, systematic review and meta-analysis.



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Abstract: In observational studies, the first step is usually to explore data distribution and the baseline differences between groups. Data description includes their central tendency (e.g., mean, median, and mode) and dispersion (e.g., standard deviation, range, interquartile range). There are varieties of bivariate statistical inference methods such as Student's t -test, Mann-Whitney U test and Chi-square test, for normal, skewed and categorical data, respectively. The article shows how to perform these analyses with R codes. Furthermore, I believe that the automation of the whole workflow is of paramount importance in that (I) it allows for others to repeat your results; (II) you can easily find out how you performed analysis during revision; (III) it spares data input by hand and is less error-prone; and (IV) when you correct your original dataset, the final result can be automatically corrected by executing the codes. Therefore, the process of making a publication quality table incorporating all abovementioned statistics and P values is provided, allowing readers to customize these codes to their own needs.

Keywords: Univariate description; bivariate statistical inference; R; table; baseline characteristics; automation

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Introduction

When data are well prepared by using previously described methods such as correcting, recoding, rescaling and missing value imputation, the next step is to perform statistical description and inference (1,2). In observational studies, the first table is usually a display of descriptive statistics of overall population, as well as statistical inference for the difference between groups. This table is important in that it gives an estimate of the differences in baseline characteristics, and provides evidence for further multivariable analysis. The article first gives an overview of methods for bivariate analysis, and then provides a step-by-step tutorial on how to perform these analyses in R. Finally, I will show how to make the table automatically. This can be useful when there are a large number of variables.

Univariate description and bivariate statistical methods

Varieties of methods are available for univariate description and bivariate inference. *Table 1* displays central tendency and dispersion for different types of data. Mean and standard deviation are probably the most widely used statistics to describe normally distributed data. For skewed data, we employ median and interquartile range. For nominal data, mode can be used for description of central tendency. However, in practice we frequently describe it by the number of each category and relevant percentage. Student's *t* test is typically applied when the test statistic would follow a normal distribution (3). Mann-Whitney U test is a non-parametric test that does not require assumption of normal distribution (4). For studies with multiple groups, analysis of variance (ANOVA) may be the best choice.

Working example

In the working example, I created three types of data that are most commonly encountered in practice. Nominal variables include those with multiple levels and those with two levels. Continuous variable include those with normal distribution and skewed data.

```
> set.seed(12)
> gender<-factor(rbinom(100, 1, 0.4),levels=c(0,1),labels=c("male","female"))
```

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```
> set.seed(12)
> trt<-factor(rbinom(100, 1, 0.5),levels=c(0,1),labels=c("treat","control"))
> set.seed(88)
> diagnosis<-factor(rbinom(100, 3, 0.5),levels=c(0,1,2,3),labels=c("heart failure","renal dysfunction","ARDS","trauma"))
> set.seed(88)
> age<-rnorm(100,mean=67,sd=20)
> set.seed(88)
> wbc<-round(exp(rnorm(100,mean=9,sd=0.8)))
> data<-data.frame(gender,age,trt,diagnosis,wbc)
```

In this dataset, gender is a binomial variable that is assigned by “male” or “female”. Variable *trt* is also binomial, but it is used for grouping purpose. Variable *diagnosis* is categorical variable with four levels. Variable *age* is normally distributed with mean of 67 and standard deviation of 20. The last variable *wbc* is skewed in distribution. The last line combines these variables into a single data frame.

Examination of skewness and kurtosis

Because the choice of statistical methods depends on the distribution of data, the first step is to examine the skewness of data. The distribution can be visualized using histogram (*Figure 1*).

```
> par(mfrow=c(1,2))
> hist(data$age)
> hist(data$wbc)
```

The first line called `par()` function to dictate that subsequent figures will be drawn in 1×2 array. It is for the purpose of better visualization and users can omit it in their own practices. As we can see from *Figure 1*, the distribution of *age* was symmetrical, while the variable *wbc* is skewed. However, graphic visualization only gives a hint on the distribution of data. To make formal judgment, we need statistical tests. The package *moments* provides good functions to do the task (5). Data distribution can be described by skewness and kurtosis. The former is a measure of the asymmetry of the probability distribution, and the latter is a measure of the “tailedness” of the probability distribution.

Table 1 Central tendency and dispersion for difference types of data

Data type	Central tendency	Description	Dispersion	Description	Statistical inference
Nominal	Mode	Value of highest frequency	NA	NA	Chi-square test
Skewed data	Median	Center value	Interquartile range	Difference between the upper and lower quartiles	Mann-Whitney U test
Normal distribution	Mean	Mathematical average	Standard deviation	How much deviate from the mean	Student's t-test

NA, not applicable.

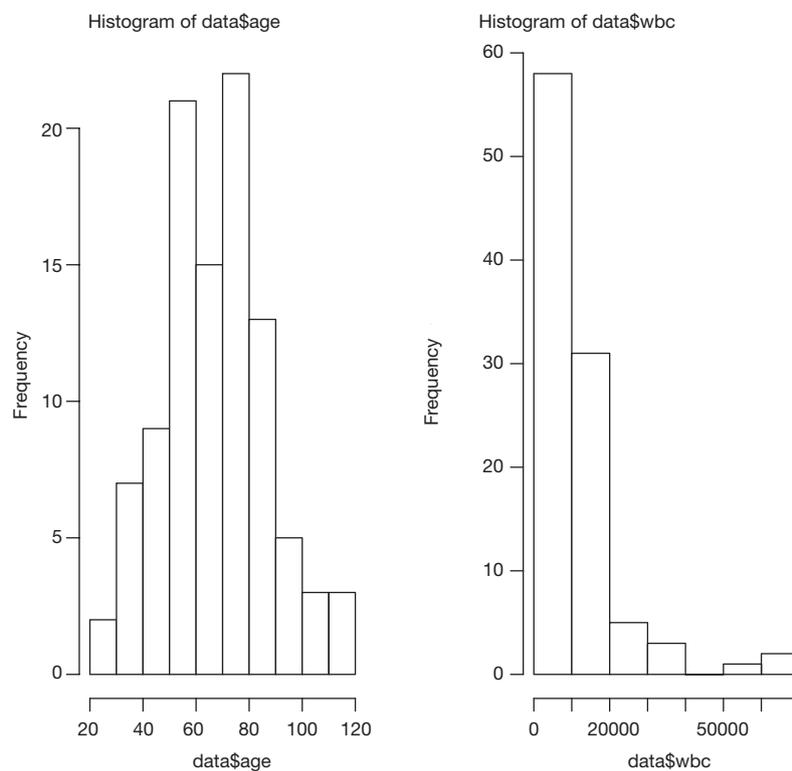


Figure 1 Histograms of variables of age and *wbc*. It appears that the distribution of *age* was symmetrical, while the variable *wbc* is skewed.

```
> install.packages("moments")
> library(moments)
> agostino.test(data$age)
```

D'Agostino skewness test

```
data: data$age
skew = 0.2462, z = 1.0571, p-value = 0.2905
alternative hypothesis: data have a skewness
```

```
> agostino.test(data$wbc)
```

D'Agostino skewness test

```
data: data$wbc
skew = 2.7039, z = 7.1426, p-value = 9.158e-13
alternative hypothesis: data have a skewness
```

The package employs the D'Agostino skewness test, details of this method can be found in reference (6). The

alternative hypothesis is that the data have a skewness. When $P < 0.05$ as for the variable *wbc*, the alternative hypothesis is accepted and there is skewness.

```
> anscombe.test(data$age)
```

Anscombe-Glynn kurtosis test

```
data: data$age
```

```
kurt = 2.8616000, z = -0.0028691, p-value = 0.9977
```

```
alternative hypothesis: kurtosis is not equal to 3
```

```
> anscombe.test(data$wbc)
```

Anscombe-Glynn kurtosis test

```
data: data$wbc
```

```
kurt = 11.463, z = 5.209, p-value = 1.898e-07
```

```
alternative hypothesis: kurtosis is not equal to 3
```

Anscombe-Glynn kurtosis test is employed to test kurtosis (6,7). Data should have kurtosis equal to 3 under the hypothesis of normality. This test incorporates such null hypothesis and is useful to detect a significant difference of kurtosis in normally distributed data. As expected, the variable *wbc* has kurtosis that is significantly different from normality.

Univariate description

Since we know the distribution of data, we need to provide central tendency and dispersion in our research. Variable *wbc* will be expressed as median and interquartile range, and *age* will be expressed as mean and standard deviation. Other categorical variables will be expressed as number and percentage.

```
> summary(age)
```

```
Min.   1st Qu. Median   Mean   3rd Qu.   Max.
26.18  52.18  68.59  67.21  78.78  118.10
```

```
> sd(age)
```

```
[1] 19.86663
```

```
> summary(wbc)
```

```
Min.   1st Qu. Median   Mean   3rd Qu.   Max.
1583  4479   8634   11360  12980  62670
```

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```
> table(diagnosis)
```

```
diagnosis
heart failure   renal dysfunction ards   trauma
11              38              37   14
```

```
> prop.table(table(diagnosis))
```

```
diagnosis
heart failure   renal dysfunction ards   trauma
0.11            0.38            0.37   0.14
```

The above codes are used for description of overall cohort. We also want to describe variables separately by the treatment group.

```
> tapply(data$wbc, data$trt, summary)
```

```
$treat
```

```
Min.   1st Qu. Median   Mean   3rd Qu.   Max.
1639  4599   8414   10170  12630  60830
```

```
$control
```

```
Min.   1st Qu. Median   Mean   3rd Qu.   Max.
1583  4508   8634   12750  13380  62670
```

```
> table(data$diagnosis, data$trt)
```

	treat	control
heart failure	5	6
renal dysfunction	20	18
ards	18	19
trauma	11	3

```
> prop.table(table(data$diagnosis, data$trt), margin=2)
```

	treat	control
heart failure	0.09259259	0.13043478
renal dysfunction	0.37037037	0.39130435
ards	0.33333333	0.41304348
trauma	0.20370370	0.06521739

The function `tapply()` “applies a function to each cell of a ragged array, that is to each (non-empty) group of values given by a unique combination of the levels of certain factors.” (8). In our example, the function `summary()` is applied to variable *wbc*, stratified

by treatment (trt). The results give summary values separately for each levels of the variable *trt*. The `table()` function is easy to use for cross tabulation.

Bivariate statistical inference

After univariate description, investigators can have a general impression on the effectiveness of a treatment. However, we still don't know whether the difference is caused by random error, or there is a real difference. Varieties of sophisticated methods are designed to answer the question.

```
> wilcox.test(wbc ~ trt, data=data)
```

Wilcoxon rank sum test with continuity correction

data: wbc by trt

W = 1166.5, p-value = 0.604

alternative hypothesis: true location shift is not equal to 0

```
> chisq.test(table(data$diagnosis,data$trt))
```

Pearson's Chi-squared test

data: table(data\$diagnosis, data\$trt)

X-squared = 4.1814, df = 3, p-value = 0.2425

```
> t.test(age ~ trt, data=data)
```

Welch Two Sample t-test

data: age by trt

t = -0.79721, df = 90.569, p-value = 0.4274

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

95 percent confidence interval:

-11.229622 4.797661

sample estimates:

mean in group treat	mean in group control
65.72955	68.94553

In above codes, the functions `wilcox.test()`, `chisq.test()` and `t.test()` are employed for skewed, categorical and normal data, respectively. The outputs of these functions include the name of the test, dataset, statistics and P value. These values can be assigned to an object for further use.

Making publication style table automatically

It is easy to copy and paste the above statistical outputs into a table in Microsoft Word when there are a limited number of variables. However, it is a tedious task when variables expand to dozens. Furthermore, making a blank table and input values by hand is prone to error. We may take the advantage of R that it allows for customized codes to automate the process of table making. It also allows to round number to desired decimal places.

```
> overall.age<-paste(round(mean(data$age),1),"±",round(sd(data$age),1))
```

```
> trt.age<-paste(round(t.test(age ~ trt, data=data)$estimate[1],1), "±",round(tapply(data$age, data$trt, sd)[1],1))
```

```
> contrl.age<-paste(round(t.test(age ~ trt, data=data)$estimate[2],1), "±",round(tapply(data$age, data$trt, sd)[2],1))
```

```
> age.p<-round(t.test(age ~ trt, data=data)$p.value,2)
```

```
> row.age<-c(overall.age,trt.age,contrl.age,age.p)
```

Many journals require that description of a variable should be put in a single cell, thus we need to use character vector to store the output in the form like "mean ± SD". The `paste()` function can connect mean and standard deviation by using the symbol "±". The `round()` function is used to save only one decimal place. Skewed data can be store in a similar way.

```
> overall.wbc<-paste(summary(data$wbc)[3],",",summary(data$wbc)[2],"~",summary(data$wbc)[5],",")
```

```
> wbc.trt.all<-tapply(data$wbc, data$trt, summary)$treat
```

```
> wbc.control.all<-tapply(data$wbc, data$trt, summary)$control
```

```
> trt.wbc<-paste(wbc.trt.all[3],",",wbc.trt.all[2],"~",wbc.trt.all[5],",")
```

```
> contrl.wbc<-paste(wbc.control.all[3],",",wbc.control.all[2],"~",wbc.control.all[5],",")
```

```
> wbc.p<-round(wilcox.test(wbc ~ trt, data=data)$p.value,2)
```

```
> row.wbc<- c(overall.wbc,trt.wbc,contrl.wbc,wbc.p)
```

This time I break the whole work into several pieces to make it clearer. The first line calculates the overall mean

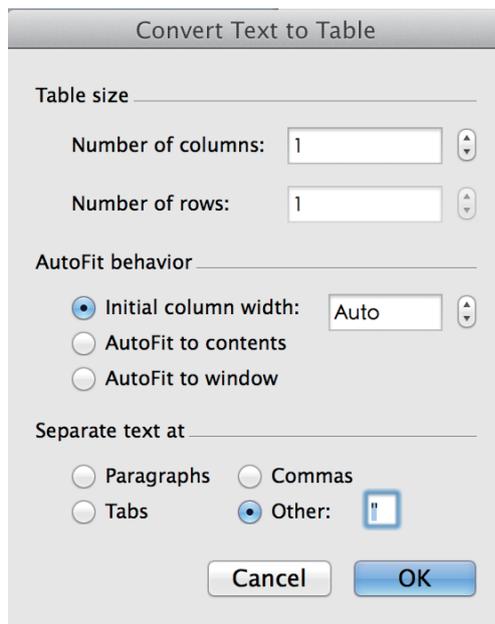


Figure 2 Settings in Microsoft Word to convert text to table. Note that the double quote mark is used to separate text.

and standard deviation, and put them to a single cell. The second and third lines calculate the summary statistics for the treatment and control groups, respectively. Because not all summary statistics are wanted, we extracted the second, third and fifth values, which represent the first quartile, median and third quartile values. The last line combines all statistics into a character vector.

```
> overall.gender<-paste(table(data$gender)[1],("prop.
table(table(data$gender))[1]*100,"%",""))
> trt.gender<-paste(table(data$gender,data$trt)
[1],("round(prop.table(table(data$gender,data$trt),mar
gin=2)[1,3])*100,"%",""))
> contrl.gender<-paste(table(data$gender,data$trt)
[3],("round(prop.table(table(data$gender,data$trt),mar
gin=2)[3,3])*100,"%",""))
> p.gender<-round(chisq.test(table(data$gender,data$tr
t))$p.value,2)
> row.gender<-c(overall.gender,trt.gender,contrl.
gender,p.gender)
```

Next we need to combine all row variables into a matrix.

```
> table<-rbind(row.age,row.gender,row.wbc)
```

```
> table
      [,1]      [,2]      [,3]      [,4]
row.age "67.2 ±    "65.7 ± 18.7" "68.9 ± 21.2" "0.43"
      19.9"
row.    "62 ( 62 % ) "34 ( 63 % ) "28 ( 60.9 % ) "0.99"
gender  "
row.    "8634 ( 4479"8414 ( 4599 "8634 ( 4508 ~"0.6"
wbc     ~ 12980 ) " ~ 12630 ) " 13380 ) "
```

The matrix output appears nearly what we want. However, the column and row names are not exactly meet the requirements for submission. We can rename them easily. For the column name I added a new character vector so that each of the names can have a double quote.

```
> row.names(table)<-c("Age (years)","Gender
(male,%)","WBC/ul")
> table.pub<-rbind(c("Overall","Treatment","Control","p
value"),table)
> table.pub
      [,1]      [,2]      [,3]      [,4]
"Overall" "Treatment" "Control" "p
value"
Age       "67.2 ±    "65.7 ± 18.7" "68.9 ± 21.2" "0.43"
(years)  19.9"
Gender   "62 ( 62 % ) "34 ( 63 % ) "28 ( 60.9 % "0.99"
(male,%) "
          ) "
WBC/ul   "8634 (    "8414 ( 4599 "8634 ( 4508 "0.6"
         4479 ~    ~ 12630 ) " ~ 13380 ) "
         12980 ) "
```

There are double quotes for each value, which is not the format for a publication quality table. The next task is done in Microsoft Word (MS). Users can copy the table from R console to MS and use the “convert text to table” function of the Word processor. In the “separate text at” option, you can use double quotes as the symbol to separate text. After click “OK” button, the double quotes mark will be replaced by lines forming cells of a table (*Figure 2*). Creating table in this way avoids you from copy and paste values one by one, which is less likely to make errors. Furthermore, because you have recorded every step for making the table in R code, you and others can reproduce the process. This is very important during revision. The rule of thumb in data management and statistical analysis is to make your results exactly reproducible.

Summary

The article provides a gentle introduction to univariate statistical description and bivariate statistical inference, which is typically the first step in exploring data. Statistical description includes statistics for central tendency such as mode, mean, median. Dispersion includes standard deviation, range, and interquartile range. They are applied to different types of data. Also, there are several statistical inference methods. They are Student's *t*-test, Mann-Whitney U test and Chi-square test. The results of these analyses should be put into a table for publication or conference presentation. The process can be automated by using R code, which makes the process easily reproducible by others and in subsequent revisions.

Acknowledgements

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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