Statistical methods for assessing agreement between two methods of clinical measurement

Solutions

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28 November 2024

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This document provides detailed solutions to the tasks set in the **Statistical methods for assessing agreement between two methods of clinical measurement** exercise set of the **Open and Reproducible Science in R** module of the **MSc in International Health and Tropical Medicine**.

1 Introduction to the exercise

The following tasks have been setup to help students get familiar with functional programming in R.

The students are expected to go through the tasks and appropriately write R code/script to fulfill the tasks and/or to answer the question/s being asked within the tasks. R code/script should be written inside a single R file named ba.R and saved in the project's root directory.

This exercise is based on:

Bland, J. M. & Altman, Douglas G. Statistical Methods For Assessing Agreement Between Two Methods Of Clinical Measurement. Lancet 327, 307–310 (1986).

The dataset used in the paper can be accessed from the teaching_datasets repository. The URL to the .dat file is https://raw.githubusercontent.com/OxfordIHTM/teaching_datasets/main/ba.dat.

The ba.dat dataset contains peak expiratory flow rate (PEFR) measurements (in litres per minute) taken with a Wright peak flow metre (Wright variable) and a Mini-Wright peak flow metre (Mini variable). This is the same data that is presented in the referenced Lancet article above.

2 Task 1: Read the dataset

This task is asking for the learner to create a function that would do the following:

- 1. Download the ba.dat file from the provided download link/URL; and,
- 2. Read that data into R.

To create this function, we can use already existing functions that does each step separately. For downloading files from the internet, there is a function called download.file(). For reading a text dataset, we can look at the read.table() family of functions.

2.1 Downloading files from the internet

The download.file() is the most straightforward function available in base R for downloading files from the internet. The basic syntax for the function is shown below:

- ① Provide the download link/URL for your file. For this task, it would be https://raw.githubusercontent.com/OxfordIHTM/teaching_datasets/main/ba.dat. Note that download link/URL should be enclosed in quotes.
- ② Provide the file path to where the file should be downloaded. The instructions specifically said that this should be downloaded into the data directory of the project and for the name, we just use the same name of the data file.

The arguments url and destfile are the minimum required arguments to specify. When you run this line of code, you should expect the ba.dat file to be downloaded into the data directory. You can check this by issuing the following command on the R console:

```
list.files("data")
[1] "ba.dat"
```

which shows that a file called ba.dat can be found inside the data directory of this project.

2.2 Reading text data

2.2.1 Reading text data after downloading

The read.table() function can be used to read the ba.dat file. After the data has been downloaded, it should be available in the data directory of our project. With this, we can use the read.table() function as follows:

```
read.table(
  file = "data/ba.dat",
  header = TRUE,
  sep = " "
)
```

- ① Specify the file path to the dataset. In our case, the dataset has been downloaded into the data directory so the relative file path to the data is data/ba.dat.
- ② Specify whether the dataset being read has variable names or column names in the first row. In our case, the ba.dat dataset has variable names included (as described in the instructions). So, we specify header = TRUE.

(3) Specify the value separators used in the dataset being read. The ba.dat dataset uses whitespace (" ") to separate values. So we specify sep = " ".

When we run this line of code, we get:

```
Wright Mini
      494
1
            512
2
      395
            430
3
      516
            520
      434
4
            428
5
      476
            500
6
      557
            600
7
      413
            364
8
      442
            380
9
      650
            658
10
      433
            445
      417
            432
11
12
      656
            626
13
      267
            260
14
      478
            477
15
      178
            259
      423
            350
16
17
      427
            451
```

We get a data.frame with 17 rows and 2 columns of data.

2.2.2 Reading text data without downloading

The read.table() family of functions allow for reading of text data direct from a download link/URL without having to download the data first. The file argument in the read.table() family of functions accepts URL of a text data file. The function then reads the data directly from that URL. This functionality is useful for when downloading of data is not needed or if there are rules with regard to downloading and/or keeping of the required dataset. However, it should be noted that reproducibility using a link to read data directly into R depends on whether the URL link is a permanent link that will not change over time.

To read the ba.dat dataset directly into R without downloading first, we use the following code:

```
read.table(
   file = "https://raw.githubusercontent.com/OxfordIHTM/teaching_datasets/main/ba.dat",
   header = TRUE,
   sep = " "
```

which gives:

```
Wright Mini
1
       494
            512
2
       395
            430
3
       516
            520
4
       434
             428
5
       476
            500
6
       557
             600
7
            364
       413
8
       442
            380
9
       650
             658
10
       433
            445
       417
            432
11
12
       656
            626
13
       267
             260
14
       478
            477
15
       178
            259
16
       423
             350
17
       427
            451
```

This is the same output as the earlier approach.

2.2.3 Function to download and then read the dataset

Now that we know how to use the download.file() and the read.table() functions, we can now use them into creating a function that downloads the data and then reads it. A basic implementation of this function will look like this:

```
read_ba_data <- function(url, destfile) {
   download.file(url = url, destfile = destfile)

read.table(file = destfile, header = TRUE, sep = " ")
}</pre>
```

- ① We set a function name of read_ba_data() and use arguments for url and destfile which are the two required arguments for download.file(). The destfile argument will then be used as the specification for the file argument for the path to the file to read in the read.table() function.
- ② Use the url and destfile argument specification to supply corresponding input values to the download.file() function.
- (3) Use the destfile argument specification to supply input value to the read.table() function. Specifications for header and sep arguments are hardcoded as it assumes that the ba.dat file has a header and uses " " as value separator.

We can then try this function to see if it gives us the expected outputs.

```
read_ba_data(
   url = "https://raw.githubusercontent.com/OxfordIHTM/teaching_datasets/main/ba.dat",
   destfile = "data/ba.dat"
)
```

which produces the following result:

```
Wright Mini
1
      494
            512
2
      395
            430
3
      516
            520
4
      434
            428
5
      476
            500
6
      557
            600
7
      413
            364
8
      442
            380
      650
            658
10
      433
            445
      417
11
            432
12
      656
            626
13
      267
            260
14
      478
            477
15
      178
            259
16
      423
            350
17
      427
            451
```

The same output is produced as earlier when the dataset was read into R. To check that the download component worked, we check if the ba.dat dataset is in the data directory of the project.

```
list.files("data")
[1] "ba.dat"
```

The ba.dat file is in the data directory. The read_ba_data() function works as expected.

2.2.4 Function to conditionally download dataset and then read the dataset

The read_ba_data() function is working the way we expect and need it to.

However, we can still consider adding some other features/functionalities that can make the function work more efficiently. For example, depending on our context and our requirements, we might want to just read the ba.dat dataset directly from the URL without downloading

it. So, we probably would like to give the user of our function the ability to decide whether the file should be downloaded and then read or should just be read into R directly. For, this, we can refactor the earlier function as follows:

- ① Use an argument called download which takes in logical values (TRUE or FALSE). If TRUE, then the function should download the dataset in the specified destfile. If FALSE, then the dataset is read directly from the url.
- (2) Create a conditional if() statement based on whether download argument is TRUE or FALSE. If TRUE, then the function should download the dataset in the specified destfile.
- (3) If the download conditions is FALSE, then the destfile argument is specified with the url value so that the dataset is read directly from the url.

To test that this updated read_ba_data() function works as expected, we first remove the ba.dat file that we have already downloaded earlier by using the following commands in the R console:

```
file.remove("data/ba.dat")
[1] TRUE
```

Then, we check whether it has indeed been removed:

```
file.exists("data/ba.dat")
```

[1] FALSE

The ba.dat file doesn't exist in the data directory.

We then test the updated read_ba_data() function first with download = FALSE as follows:

① Set download = FALSE so that ba.dat is read directly into R without downloading. Since no download of data will be performed, there is no need to specify the destfile argument.

This code outputs the following:

	Wright	Mini
1	494	512
2	395	430
3	516	520
4	434	428
5	476	500
6	557	600
7	413	364
8	442	380
9	650	658
10	433	445
11	417	432
12	656	626
13	267	260
14	478	477
15	178	259
16	423	350
17	427	451

which is the same output as the earlier function.

We then test whether or not the ba.dat file is present in the data directory. Our expectation is that the ba.dat file is not to be found there. We test as follows:

```
file.exists("data/ba.dat")
```

[1] FALSE

The ba.dat file is not found in the data directory. The updated read_ba_data() function works as expected.

2.2.5 Function to conditionally download dataset and then read the dataset - overwrite

The updated read_ba_data() function is working the way we expect and need it to.

However, we can still consider adding some conditionalities that can make the function work more efficiently. For example, once we have used the current read_ba_data() function with download = TRUE specification, the ba.dat file should already be in our data directory. Since this dataset is not expected to change anymore¹, we might want to update the current read_ba_data() function such that it will not overwrite an existing download of ba.dat if download = TRUE. This is useful as we don't have to repeat a download operation if the file is already present in our data directory. To implement this functionality, the read_ba_data() function can be updated as follows:

```
read_ba_data <- function(url,</pre>
                          download = TRUE,
                          destfile,
                          overwrite = FALSE) {
                                                                             (1)
  ## If download = TRUE, download dataset
  if (download) {
    ## If overwrite = TRUE, download dataset
    if (overwrite) {
                                                                             (2)
      download.file(url = url, destfile = destfile)
    } else {
    ## If overwrite = FALSE, check if destfile exists before downloading
      if (!file.exists(destfile)) {
                                                                             (3)
        download.file(url = url, destfile = destfile)
      }
    }
  } else {
  ## If download = FALSE, set destfile as url link
    destfile <- url
  ## Read dataset
  read.table(file = destfile, header = TRUE, sep = " ")
}
```

- (1) Use overwrite argument that takes on logical (TRUE or FALSE) value so that user can specify whether they want the function to overwrite an existing file specified by destfile.
- (2) If download = TRUE and overwrite = TRUE, download of the dataset is performed regardless of whether it is already present.

¹This dataset is a teaching dataset and is provided by Bland and Altman in their paper. It is very reasonable to expect that no changes will happen to this dataset in the future.

(3) If download = TRUE and overwrite = FALSE (default), a check is performed whether the file path specified in destfile exists. If it doesn't exist, then download of the dataset is performed. If the file exists, then dataset is not downloaded.

We can now test whether the function works as expected. From the earlier example, we have the previous download of the ba.dat file and then ran the previous function with download = FALSE. So, no ba.dat file is currently found in the data directory. To test whether overwrite = FALSE works, we use the updated function as follows

```
read_ba_data(
  url = "https://raw.githubusercontent.com/OxfordIHTM/teaching_datasets/main/ba.dat",
  download = TRUE,
                                                                                 1
  destfile = "data/ba.dat",
  overwrite = FALSE
)
and then we get:
   Wright Mini
      494
1
            512
2
      395
            430
3
      516
            520
      434
            428
4
5
      476
            500
6
      557
            600
7
      413
            364
8
      442
            380
9
      650
            658
10
      433
            445
11
      417
            432
12
      656
            626
13
      267
            260
14
      478
            477
15
      178
            259
16
      423
            350
17
      427
            451
```

We get the data read into R and then we expect that the download process happened because download = TRUE even though overwrite = FALSE because the ba.dat file is not present in data directory. We check this by

```
file.exists("data/ba.dat")
[1] TRUE
```

The ba.dat file was found in the data directory of the project.

Now that the ba.dat file is back in the data directory, we can test the overwrite = FALSE argument again. We expect that the read_ba_data() will not re-download the ba.dat dataset. Instead, it will just read what is already available in the data directory.

We get the data read into R and during the running of the code, we notice that no console message relating to download were showing with the whole process taking relatively quicker than earlier.

```
Wright Mini
      494
           512
1
2
      395
            430
3
      516
            520
4
      434
            428
5
      476
            500
6
      557
            600
7
      413
            364
      442
            380
8
9
      650
            658
            445
10
      433
11
      417
            432
12
      656
            626
13
      267
            260
14
      478
            477
15
      178
            259
16
      423
            350
17
      427
            451
```

Then we can test the overwrite = TRUE argument. We expect that the read_ba_data() will download the ba.dat dataset regardless of whether the ba.dat is found in the data directory.

We get the data read into R and during the running of the code, we notice that on the console we see messages relating to the download process were showing (see console output 1) with the whole process taking relatively longer than earlier.

Listing 1 Console output showing downloading process ongoing

downloaded 166 bytes

```
Wright Mini
      494
1
           512
2
      395
            430
3
      516
            520
4
      434
            428
5
      476
            500
6
      557
            600
7
      413
            364
8
      442
            380
9
      650
            658
10
      433
            445
      417
            432
11
12
      656
            626
13
      267
            260
14
      478
            477
            259
15
      178
16
      423
            350
17
      427
            451
```

The updated read_ba_data() function is working as expected. We use it to create a data object called ba_data.

```
ba_data <- read_ba_data(
   url = "https://raw.githubusercontent.com/OxfordIHTM/teaching_datasets/main/ba.dat",
   destfile = "data/ba.dat"
)
which results in:
ba_data
   Wright Mini
1   494  512</pre>
```

```
2
       395
            430
3
       516
            520
4
       434
            428
5
       476
            500
6
       557
            600
7
       413
            364
8
       442
            380
9
       650
            658
       433
            445
10
       417
            432
11
12
       656
            626
13
       267
            260
14
       478
            477
15
       178
            259
16
       423
            350
17
       427
            451
```

3 Task 2: Calculate the metrics needed for a Bland and Altman plot

The different metrics used to consruct a Bland and Altman plot are:

- Mean of the per subject measurements made by the Wright and the Mini-Wright;
- Difference between the per subject measurements made by the Wright and the Mini-Wright;
- Mean of the difference between the per subject measurements made by the Wright and the Mini-Wright; and,
- Lower and upper limits of agreement between the per subject measurements made by the Wright and the Mini-Wright.

We can approach this task in five different ways.

3.1 Function to calculate Bland and Altman metrics - vectorised approach

The vectorised approach calculates each metric as $vectors^2$ and then concatenates them into a list³. The following function shows this approach:

²A vector is essentially a collection of elements of the same data type, arranged in a one-dimensional array.

³A list is a data structure that can store elements of different types. Unlike vectors, which are homogenous (all elements must be of the same type), lists are heterogeneous and can hold elements such as numbers, strings, vectors, other lists, and even functions.

```
calculate_ba_metrics <- function(ba_data) {</pre>
                                                                                (1)
  ## Get per row mean of measurements
 mean_values <- (ba_data$Wright + ba_data$Mini) / 2</pre>
                                                                                (2)
 ## Get per row difference of measurements
 differences <- ba_data$Wright - ba_data$Mini</pre>
                                                                                (3)
  ## Mean of the differences of measurements
 mean_differences <- mean(differences)</pre>
                                                                                (4)
 ## Upper and lower limits of agreement
 upper_limit <- mean_differences + 1.96 * sd(differences)</pre>
                                                                                (5)
 lower_limit <- mean_differences - 1.96 * sd(differences)</pre>
 ## Concatenate metrics into a named list
 list(
                                                                                (6)
    mean_values = mean_values,
    differences = differences,
    mean differences = mean differences,
    upper_limit = upper_limit,
    lower_limit = lower_limit
 )
```

- (1) Name the function calculate_ba_metrics() and use an argument ba_data which is the data frame of the dataset we downloaded and read in the first task.
- (2) Calculate the per row mean of the two measurements and assign it to the mean_values
- (3) Calculate the per row difference between the two measurements and assign it to the differences object.
- (4) Calculate the mean of the per row differences and assign it to the mean differences object.
- (5) Calculate the upper and lower limits of agreement and assign them to the upper_limit and lower_limit objects respectively.
- (6) Concatenate all the calculated values into a named list.

We use this function as follows:

```
calculate_ba_metrics(ba_data)
```

which gives the following output:

```
$mean_values
```

}

```
[1] 503.0 412.5 518.0 431.0 488.0 578.5 388.5 411.0 654.0 439.0 424.5 641.0
[13] 263.5 477.5 218.5 386.5 439.0
```

```
$differences
[1] -18 -35 -4 6 -24 -43 49 62 -8 -12 -15 30 7 1 -81 73 -24
$mean_differences
[1] -2.117647
$upper_limit
[1] 73.86201
$lower_limit
[1] -78.0973
```

We see the named list structure of the output with the mean_values and the differences being vectors whilst the rest of the metrics are single values.

3.2 Function to calculate Bland and Altman metrics - data.frame approach

The data frame approach outputs each metric as vectors and concatenates them into the input dataset. The function using this approach can look like this:

```
calculate_ba_metrics <- function(ba_data) {</pre>
  ## Get per row mean of measurements and add to ba_data
 ba_data$mean_values <- (ba_data$Wright + ba_data$Mini) / 2</pre>
                                                                               1
 ## Get per row difference of measurements and add to ba_data
 ba_data$differences <- ba_data$Wright - ba_data$Mini</pre>
                                                                               (2)
  ## Mean of the differences of measurements
 ba_data$mean_differences <- mean(ba_data$differences)</pre>
                                                                               (3)
 ## Upper and lower limits of agreement
 ba_data$upper_limit <- ba_data$mean_differences + 1.96 *</pre>
                                                                               (4)
    sd(ba_data$differences)
 ba_data$lower_limit <- ba_data$mean_differences - 1.96 *</pre>
    sd(ba_data$differences)
 ## Return ba_data
 ba_data
}
```

- ① The per row mean of measurements are calculated and added as a new column in the input dataset.
- (2) The per row difference in measurements are calculated and added as a new column in the input dataset.

- (3) The mean of the difference in measurements is calculated and added as a new column in the input dataset. Because this value is a single value, it is repeated per row of the input data.
- (4) The upper and lower limits of agreement in measurements are calculated and are each added as new columns in the input dataset. Because these values correspond to single values, they are repeated per row of the input data.

We use this function as follows:

```
calculate_ba_metrics(ba_data)
```

which gives the following output:

	Wright	Mini	mean_values	differences	mean_differences	upper_limit	lower_limit
1	494	512	503.0	-18	-2.117647	73.86201	-78.0973
2	395	430	412.5	-35	-2.117647	73.86201	-78.0973
3	516	520	518.0	-4	-2.117647	73.86201	-78.0973
4	434	428	431.0	6	-2.117647	73.86201	-78.0973
5	476	500	488.0	-24	-2.117647	73.86201	-78.0973
6	557	600	578.5	-43	-2.117647	73.86201	-78.0973
7	413	364	388.5	49	-2.117647	73.86201	-78.0973
8	442	380	411.0	62	-2.117647	73.86201	-78.0973
9	650	658	654.0	-8	-2.117647	73.86201	-78.0973
10	433	445	439.0	-12	-2.117647	73.86201	-78.0973
11	417	432	424.5	-15	-2.117647	73.86201	-78.0973
12	656	626	641.0	30	-2.117647	73.86201	-78.0973
13	267	260	263.5	7	-2.117647	73.86201	-78.0973
14	478	477	477.5	1	-2.117647	73.86201	-78.0973
15	178	259	218.5	-81	-2.117647	73.86201	-78.0973
16	423	350	386.5	73	-2.117647	73.86201	-78.0973
17	427	451	439.0	-24	-2.117647	73.86201	-78.0973

We see the data.frame structure of the output with new columns/variables for each of the calculated metric and the repeated per row values for the mean_differences, upper_limit, and lower_limit.

3.3 Function to calculate Bland and Altman metrics - combined approach

The structure of the output (either list or data.frame) each has their pros and cons. A list structure is relatively more flexible and can be transformed in many ways whilst the data.frame structure is ideal for use in functions that require a data.frame input (i.e., ggplot2 for plotting). With this in mind, a combined approach that gives users an option between a vectorised or a data.frame approach can be useful and have a broader and more generalised usage.

This function can be implemented as follows:

```
calculate_ba metrics <- function(ba_data, type = c("list", "df")) {</pre>
                                                                                 (1)
  type <- match.arg(type)</pre>
                                                                                 (2)
  mean_values <- (ba_data$Wright + ba_data$Mini) / 2</pre>
                                                                                 (3)
  differences <- ba_data$Wright - ba_data$Mini</pre>
  mean_differences <- mean(differences)</pre>
  upper_limit <- mean_differences + 1.96 * sd(differences)</pre>
  lower_limit <- mean_differences - 1.96 * sd(differences)</pre>
  if (type == "list") {
                                                                                 (4)
    list(
      mean_values = mean_values,
      differences = differences,
      mean_differences = mean_differences,
      upper_limit = upper_limit,
      lower_limit = lower_limit
    )
  } else {
    data.frame(
      ba_data, mean_values, differences, mean_differences,
      upper_limit, lower_limit
    )
 }
}
```

- ① Use an argument called type which can be specified as either list or df (short for data.frame).
- (2) The function match.arg() matches the input value for type to the choices allowed and checks whether it is specified correctly. If type not specified, match.arg() uses the first value (list) as the default.
- (3) Calculate each of the metrics like before.
- (4) Based on what type is, the metrics are concatenated into a list or into a data.frame.

We use this function as follows to output a list:

```
calculate_ba_metrics(ba_data)
```

which gives the following output:

```
$mean_values
```

```
[1] 503.0 412.5 518.0 431.0 488.0 578.5 388.5 411.0 654.0 439.0 424.5 641.0 [13] 263.5 477.5 218.5 386.5 439.0
```

\$differences

```
[1] -18 -35 -4 6 -24 -43 49 62 -8 -12 -15 30 7 1 -81 73 -24
```

```
$mean_differences
[1] -2.117647

$upper_limit
[1] 73.86201

$lower_limit
[1] -78.0973
```

We use this function as follows to output a data.frame:

```
calculate_ba_metrics(ba_data, type = "df")
```

which gives the following output:

	Wright	Mini	${\tt mean_values}$	${\tt differences}$	${\tt mean_differences}$	${\tt upper_limit}$	<pre>lower_limit</pre>
1	494	512	503.0	-18	-2.117647	73.86201	-78.0973
2	395	430	412.5	-35	-2.117647	73.86201	-78.0973
3	516	520	518.0	-4	-2.117647	73.86201	-78.0973
4	434	428	431.0	6	-2.117647	73.86201	-78.0973
5	476	500	488.0	-24	-2.117647	73.86201	-78.0973
6	557	600	578.5	-43	-2.117647	73.86201	-78.0973
7	413	364	388.5	49	-2.117647	73.86201	-78.0973
8	442	380	411.0	62	-2.117647	73.86201	-78.0973
9	650	658	654.0	-8	-2.117647	73.86201	-78.0973
10	433	445	439.0	-12	-2.117647	73.86201	-78.0973
11	417	432	424.5	-15	-2.117647	73.86201	-78.0973
12	656	626	641.0	30	-2.117647	73.86201	-78.0973
13	267	260	263.5	7	-2.117647	73.86201	-78.0973
14	478	477	477.5	1	-2.117647	73.86201	-78.0973
15	178	259	218.5	-81	-2.117647	73.86201	-78.0973
16	423	350	386.5	73	-2.117647	73.86201	-78.0973
17	427	451	439.0	-24	-2.117647	73.86201	-78.0973

3.4 Function to calculate Bland and Altman metrics - modular approach

The modular approach creates multiple functions that calculates each component metric of the Bland and Altman plot and then assembles them into one overall function. An example of how these functions might look like is shown below:

```
calculate_mean_values <- function(m1, m2) { (m1 + m2) / 2 }
calculate_diff_values <- function(m1, m2) { m1 - m2 }
calculate_mean_diff <- function(m1, m2) {</pre>
```

```
mean(calculate_diff_values(m1 = m1, m2 = m2))
}
calculate_diff_limits <- function(m1, m2) {</pre>
 differences <- calculate_diff_values(m1 = m1, m2 = m2)</pre>
 mean_differences <- calculate_mean_diff(m1 = m1, m2 = m2)</pre>
 upper_limit <- mean_differences + 1.96 * sd(differences)</pre>
 lower_limit <- mean_differences - 1.96 * sd(differences)</pre>
 c(upper_limit, lower_limit)
}
calculate_ba_metrics <- function(ba_data, type = c("list", "df")) {</pre>
  type <- match.arg(type)</pre>
 mean_values <- calculate_mean_values(m1 = ba_data$Wright, m2 = ba_data$Mini)</pre>
 differences <- calculate_diff_values(m1 = ba_data$Wright, m2 = ba_data$Mini)</pre>
 mean_differences <- calculate_mean_diff(m1 = ba_data$Wright, m2 = ba_data$Mini)</pre>
 limits <- calculate_diff_limits(m1 = ba_data$Wright, m2 = ba_data$Mini)</pre>
 if (type == "list") {
    list(
      mean_values = mean_values,
      differences = differences,
      mean_differences = mean_differences,
      upper_limit = limits[1],
      lower_limit = limits[2]
 } else {
    data.frame(
      ba_data, mean_values, differences, mean_differences,
      upper_limit, lower_limit
    )
 }
}
```

4 Task 3: Create a Bland and Altman plot

Develop a function that creates a Bland and Altman plot as described in the article.