

Name: Shailina Keshwani

Objective: To provide a simple and useful data visualization for concomitant drug use or switching.

Description: In drug utilization study we are often interested in looking at concomitant use of drugs or medication switching in our patient population. Such trend analysis is important to understand prescribing practices and drug utilization in the real-world setting. Tables are often used to describe such data, but it can be cumbersome and difficult to follow when data is too big. This issue can be resolved by using ChordDiagram function in the R software, which allows the readers to visualize such data intuitively.

The dataset provided for the demonstration of the code looks at initial antihypertensive regimens in newly diagnosed hypertension patients. It is not uncommon for these newly diagnosed hypertension patients to initiate their drug regimen with more than one anti-hypertensive medications. Therefore, it is important to know how often different anti-hypertensives are prescribed concomitantly. The frequency table containing such a data may not help the readers to know which anti-hypertensives drugs are prescribed more frequently together. Hence, ChorDiagram has the benefit to link information between two columns using frequencies. In the dataset provided we have three columns as medname1, medname2 and frequency. In the given code the column medname1 links to medname2 and the thickness of the link determines how often are they prescribed together. The provided code also helps to differentiate between the different drug classes using different colors for each anti-hypertensive class.

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User manual (R program)

Complete Code

#Install packages

```
install.packages("devtools")
```

```
devtools::install_github("mattflor/chorddiag", build_vignettes = TRUE)
```

```
library(tidyverse)
```

```
library(hrbrthemes)
```

```
library(circlize)
```

```
library(chorddiag)
```

```
library(igraph)
```

```
library(tidygraph)
```

#Import dataset

```
data <- read.csv ("your file location", header=TRUE)
```

#Step1

```
circos.clear()
```

```
circos.par(start.degree = 75, gap.degree =2, track.margin = c(-0.3, 0.3), points.overflow.warning = FALSE)
```

#Step2

#Inorder to define color according to your needs or in this case by class we need to create an object called col

```
col= c(LISINOPRIL= "plum3", "ENALAPRIL"="plum3", "BENZAEPRIIL"="plum3", #ACE inhibitors
```

```
DOXAZOSIN= "blue", #Alpha1 blocker
```

```
CLONIDINE="grey", #Alpha2 Agonist
```

```
LOSARTAN="purple", #ARB
```

```
ATENOLOL= "hotpink", CARVEDILOL="hotpink", METOPROLOL= "hotpink", LABETALOL="hotpink", PROPRANOLOL="hotpink",  
BISOPROLOL="hotpink", #Beta blockers
```

```
AMLODIPINE="powderblue", #DHPCCB
```

```
SPIRONOLACTONE="lightskyblue", #K-sparing diuretics
```

```
FUROSEMIDE='moccasin', BUMETANIDE='moccasin', #Loop diuretics
```

```
DILTIAZEM="brown", #Non-PHP CCB
```

```
HYDROCHLOROTHIAZIDE="gold",CHLORTHALIDONE="gold", # Thiazide Diuretics
```

```
HYDRALAZINE="darkgreen") #Vasodilator"
```

#Step3

Base plot

```
chordDiagram(  
  x = data,  
  grid.col = col,  
  directional = 0, #data flow  
  diffHeight = -0.04,
```

```
annotationTrack = "grid",
annotationTrackHeight = c(0.05, 0.1),
link.largest.ontop = TRUE
)
#Step4
# Add text and axis
circos.trackPlotRegion(
  track.index = 1,
  bg.border = NA,
  panel.fun = function (x, y) {
    xlim = get.cell.meta.data("xlim")
    sector.index = get.cell.meta.data("sector.index")

    # Add names to the sector.
    circos.text(
      x = mean(xlim),
      y = 1.2, #adjust space between the labels and the circle
      adj = c(0, 0.5),
      labels = sector.index,
      facing = "clockwise",
```

```
niceFacing = TRUE,
```

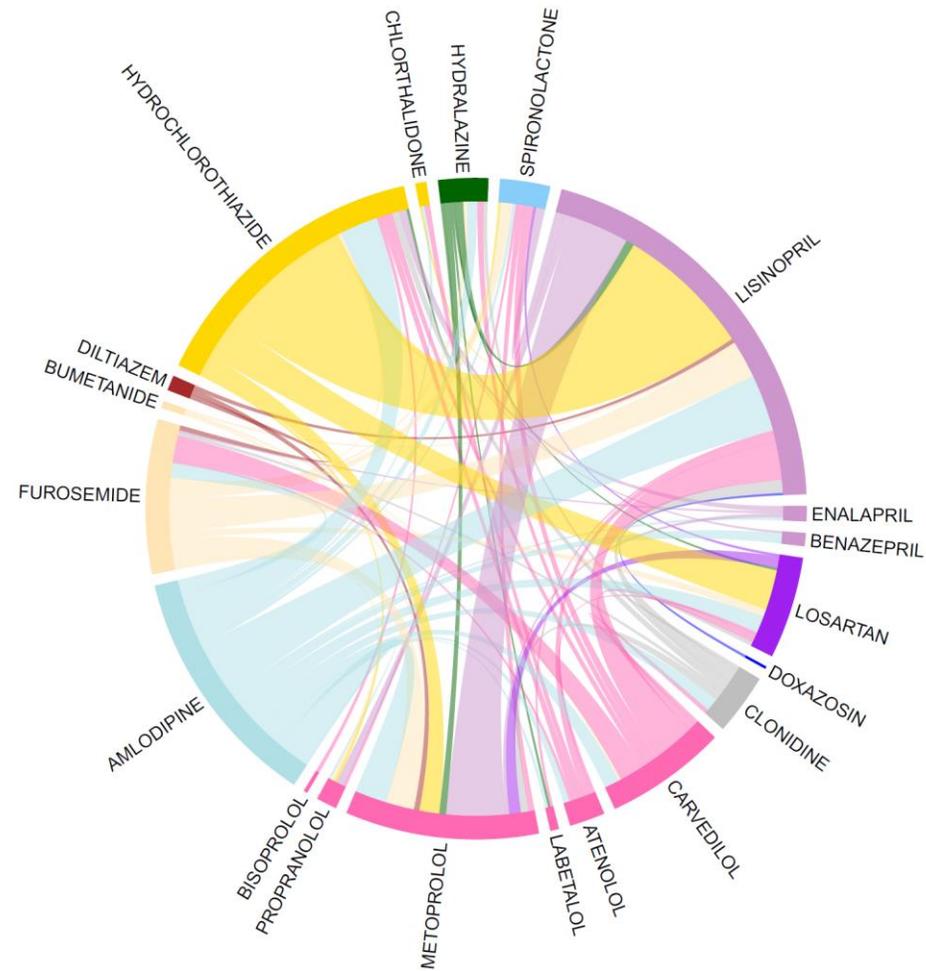
```
cex = 0.5
```

```
)
```

```
}
```

```
)
```

Figure



From the above figure we can see that hydrochlorothiazide and lisinopril are most prescribed together whereas doxazosin is least prescribed concomitantly with other drugs.

Code Instructions and Demonstrations

Install packages

```
#Install packages
install.packages("devtools")
devtools::install_github("mattflor/chorddiag", build_vignettes = TRUE)
library(tidyverse)
library(hrbrthemes)
library(circlize)
library(chorddiag)
library(igraph)
library(tidygraph)
```

These are the required packages which can be installed in R using `tools> install packages`

Import dataset

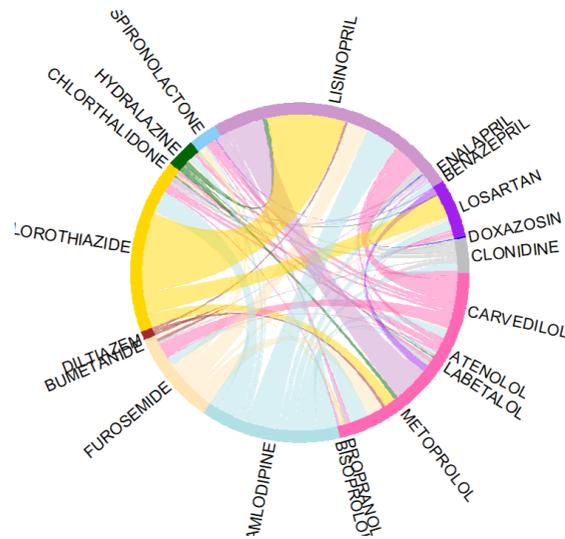
```
data <- read.csv("your file location", header=TRUE)
```

Step1

First, we need to use `circos.par` parameter to set the circular layout of the plot `start.degree` helps to rotate the circle in clockwise fashion `track.margin` determines the size of the circle and `gap.degree` determines the gap between two drugs

Example1

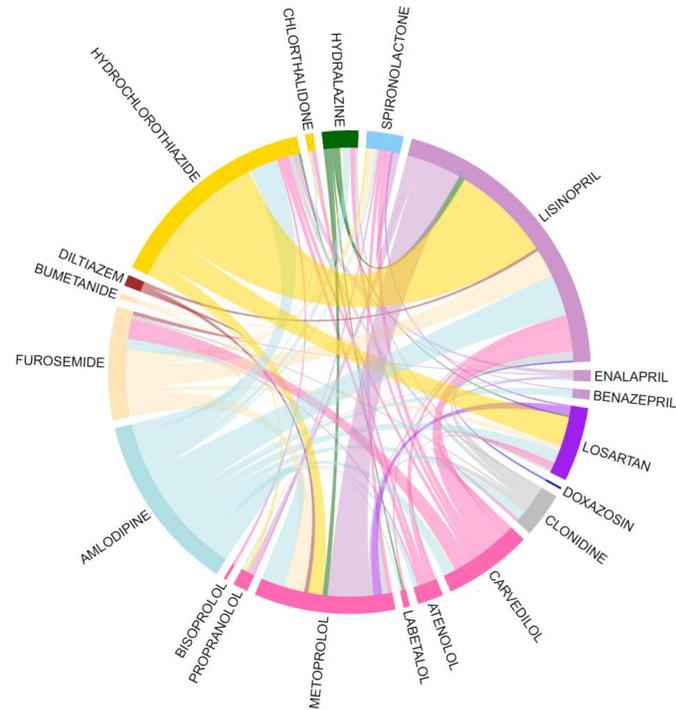
```
#Step1
circos.clear()
circos.par(start.degree = 120, gap.degree = 0, track.margin = c(-0.3, 0.3), points.overflow.warning = FALSE)
```



In the above example we can see that some names are not properly displayed and there is no gap between the drugs

Example 2

```
#Step1  
circos.clear()  
circos.par(start.degree = 75, gap.degree = 2, track.margin = c(-0.3, 0.3), points.overflow.warning = FALSE)
```



In this we can see that all the names are properly displayed, and the circle is rotate by 75 degrees with gaps between the drugs

Step2

```
#Step2
#Inorder to define color according to your needs or in this case by class we need to create an object called col
col= c(LISINOPRIL= "plum3", "ENALAPRIL"="plum3", "BENZAEPRIIL"="plum3", #ACE inhibitors
      DOXAZOSIN= "blue", #Alpha1 blocker
      CLONIDINE="grey", #Alpha2 Agonist
      LOSARTAN="purple", #ARB
      ATENOLOL= "hotpink",CARVEDILOL="hotpink", METOPROLOL= "hotpink", LABETALOL="hotpink",
      PROPRANOLOL="hotpink", BISOPROLOL="hotpink", #Beta blockers
      AMLODIPINE="powderblue", #DHPCCB
      SPIRONOLACTONE="lightskyblue", #K-sparing diuretics
      FUROSEMIDE='moccasin', BUMETANIDE='moccasin', #Loop diuretics
      DILTIAZEM="brown", #Non-PHP CCB
      HYDROCHLOROTHIAZIDE="gold",CHLORTHALIDONE="gold", # Thiazide Diuretics
      HYDRALAZINE="darkgreen" )#Vasodilator"
```

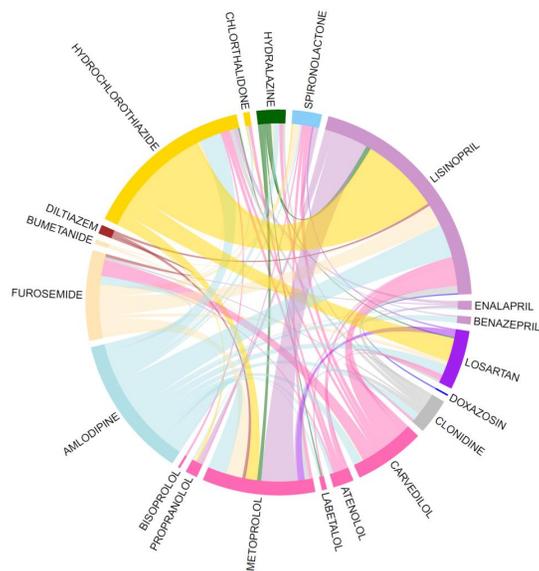
In this I have created an object called col, which will be used in the below codes. This object is used to color code drugs according to their class.

Step 3

Base plot has many functions. The important functions used here are `directional`, `direction.type`, `link.arr.type`

Example1 (Concomitant drug use)

```
#Step3
# Base plot
chordDiagram(
  x = data,
  grid.col = col,
  directional = 0, #data flow
  diffHeight = -0.04,
  annotationTrack = "grid",
  annotationTrackHeight = c(0.05, 0.1),
  link.largest.ontop = TRUE
)
```

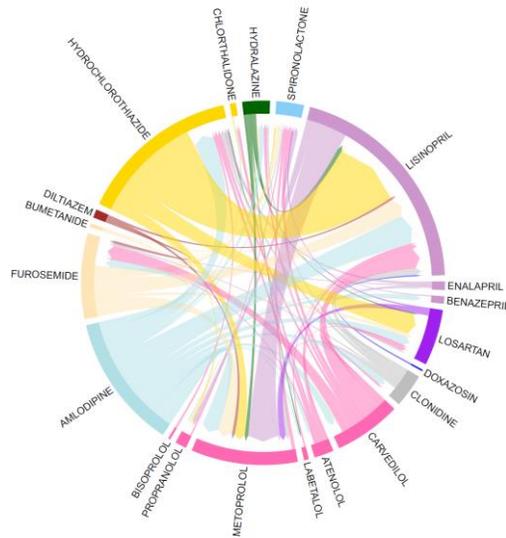


Here we look at concomitant use of drugs therefore `directional=0` with no arrows and just solid connections between the drugs.

Example 2 (Switching)

```
#Step3
# Base plot
chordDiagram(
  x = data,
  grid.col = col,
  directional = 1, #data flow
  diffHeight = -0.04,
  annotationTrack = "grid",
  direction.type = c("arrows", "diffHeight"), #arrow type
  link.arr.type = "big.arrow",
  annotationTrackHeight = c(0.05, 0.1),
  link.largest.on.top = TRUE
)
```

The same code in step 3 example1 can be modified to show switching. I have used the same data to show how switching can be demonstrated. In the below figure I have added `direction.type`, `link.arr.type` with `directional=1` this can be used to determine switching from one drug to another.



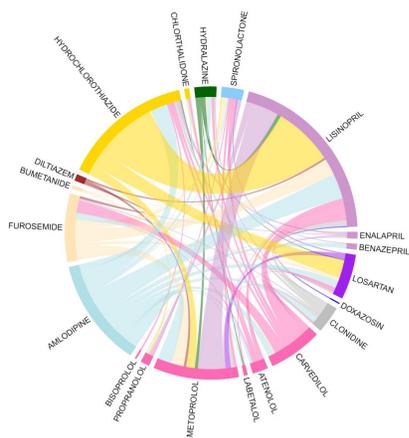
Here the arrow moving from hydrochlorothiazide to lisinopril is showing switching. (Note: The data used for switching is for demonstration purpose only. The actual data is about concomitant use)

Step 4

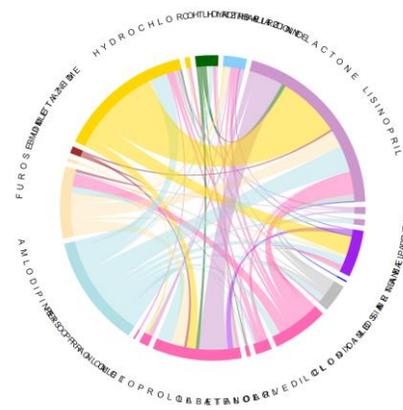
```
#Step4
# Add text and axis
circos.trackPlotRegion(
  track.index = 1,
  bg.border = NA,
  panel.fun = function(x, y) {
    xlim = get.cell.meta.data("xlim")
    sector.index = get.cell.meta.data("sector.index")

    # Add names to the sector.
    circos.text(
      x = mean(xlim),
      y = 1.2, #adjust space between the labels and the circle
      adj = c(0, 0.5),
      labels = sector.index,
      facing = "clockwise",
      niceFacing = TRUE,
      cex = 0.5
    )
  }
)
```

In this step we can adjust the space between the label and plot and also change the facing from clockwise to bending inside (bending.inside). Many other functions can also be changed to meet your needs



'clockwise'



'bending.inside'

Statement

This program can be made available to collaborators and if deemed of interest to others, for public download at the CoDES website