

Bios 6301: Assignment 6

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Due Thursday, 1 December, 1:00 PM

$5^{n=\text{day}}$ points taken off for each day late.

50 points total.

Submit a single knitr file (named `homework6.rmd`), along with a valid PDF output file. Inside the file, clearly indicate which parts of your responses go with which problems (you may use the original homework document as a template). Add your name as `author` to the file's metadata section. Raw R code/output or word processor files are not acceptable.

Failure to name file `homework6.rmd` or include author name may result in 5 points taken off.

Question 1

15 points

Consider the following very simple genetic model (*very* simple – don't worry if you're not a geneticist!). A population consists of equal numbers of two sexes: male and female. At each generation men and women are paired at random, and each pair produces exactly two offspring, one male and one female. We are interested in the distribution of height from one generation to the next. Suppose that the height of both children is just the average of the height of their parents, how will the distribution of height change across generations?

Represent the heights of the current generation as a dataframe with two variables, `m` and `f`, for the two sexes. We can use `rnorm` to randomly generate the population at generation 1:

```
pop <- data.frame(m = rnorm(100, 160, 20), f = rnorm(100, 160, 20))
```

The following function takes the data frame `pop` and randomly permutes the ordering of the men. Men and women are then paired according to rows, and heights for the next generation are calculated by taking the mean of each row. The function returns a data frame with the same structure, giving the heights of the next generation.

```
next_gen <- function(pop) {  
  pop$m <- sample(pop$m)  
  pop$m <- rowMeans(pop)  
  pop$f <- pop$m  
  pop  
}
```

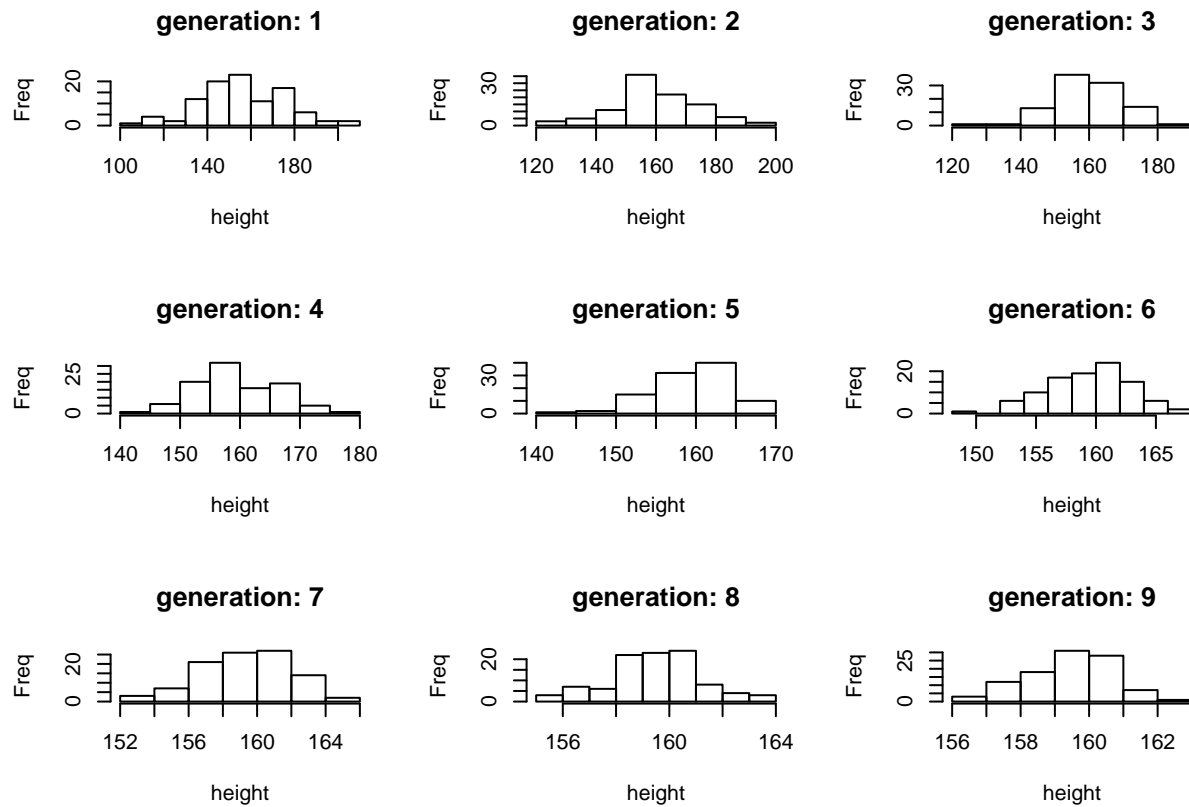
Use the function `next_gen` to generate nine generations (you already have the first), then use the function `hist` to plot the distribution of male heights in each generation (this will require multiple calls to `hist`). The phenomenon you see is called regression to the mean. Provide (at least) minimal decorations such as title and x-axis labels.

```
gen<-list()  
gen[[1]]<-pop  
par(mfrow = c(3,3))  
hist(gen[[1]]$m, main=paste("generation:",1), xlab = "height", ylab = "Freq")  
for (i in 2:9){
```

```

gen[[i]]<-next_gen(gen[[i-1]])
hist(gen[[i]]$m, main=paste("generation:",i), xlab = "height", ylab = "Freq")
}

```



Question 2

10 points

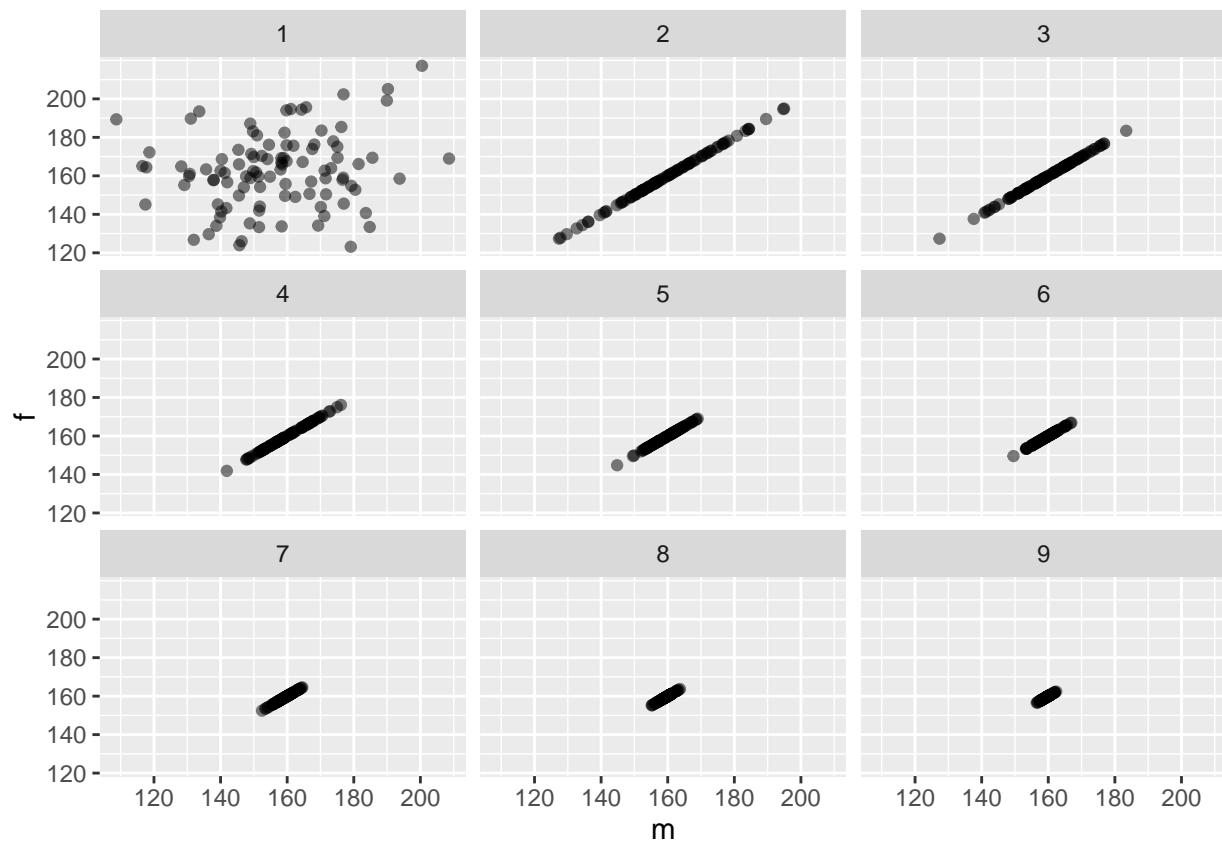
Use the simulated results from question 1 to reproduce (as closely as possible) the following plot in ggplot2.

```

library(ggplot2)
library(grid)

for(i in 1:9){
  gen[[i]]$g <- i
}
gent<-gen[[1]]
for(i in 2:9){
  gent<-rbind(gent,gen[[i]])
}
ggplot(gent,aes(x=m,y=f))+geom_point(alpha=0.5) + scale_x_continuous(breaks=seq(100,220,20)) + scale_y_

```



Question 3

10 points

You calculated the power of a study design in question #2 of assignment 3. The study has two variables, treatment group and outcome. There are two treatment groups (0, 1) and they should be assigned randomly with equal probability. The outcome should be a random normal variable with a mean of 60 and standard deviation of 20. If a patient is in the treatment group, add 5 to the outcome.

Starting with a sample size of 250, create a 95% bootstrap percentile interval for the mean of each group. Then create a new bootstrap interval by increasing the sample size by 250 until the sample is 2500. Thus you will create a total of 10 bootstrap intervals. Each bootstrap should create 1000 bootstrap samples. (4 points) Produce a line chart that includes the bootstrapped mean and lower and upper percentile intervals for each group. Add appropriate labels and a legend. (6 points)

```
t_mean<-t_up<-t_lw<-rep(0,10)
c_mean<-c_up<-c_lw<-rep(0,10)
for ( i in seq(250,2500,250)){
  sample<-rnorm(i,mean=60,sd=20)
  pre<-rbinom(i,1,0.5)
  t<-sample[pre==1]
  c<-sample[pre==0]
  t=t+5

  t_boot<-replicate(1000,mean(sample(t,size=length(t),replace=T)))
  c_boot<-replicate(1000,mean(sample(c,size=length(c),replace=T)))
  t_mean[i/250]<-mean(t)
```

```

t_up[i/250]<-quantile(t_boot,0.975)
t_lw[i/250]<-quantile(t_boot,0.025)
c_mean[i/250]<-mean(c)
c_up[i/250]<-quantile(c_boot,0.975)
c_lw[i/250]<-quantile(c_boot,0.025)
}

```

You may use base graphics or ggplot2. It should look similar to this (in base).

Here's an example of how you could create transparent shaded areas.

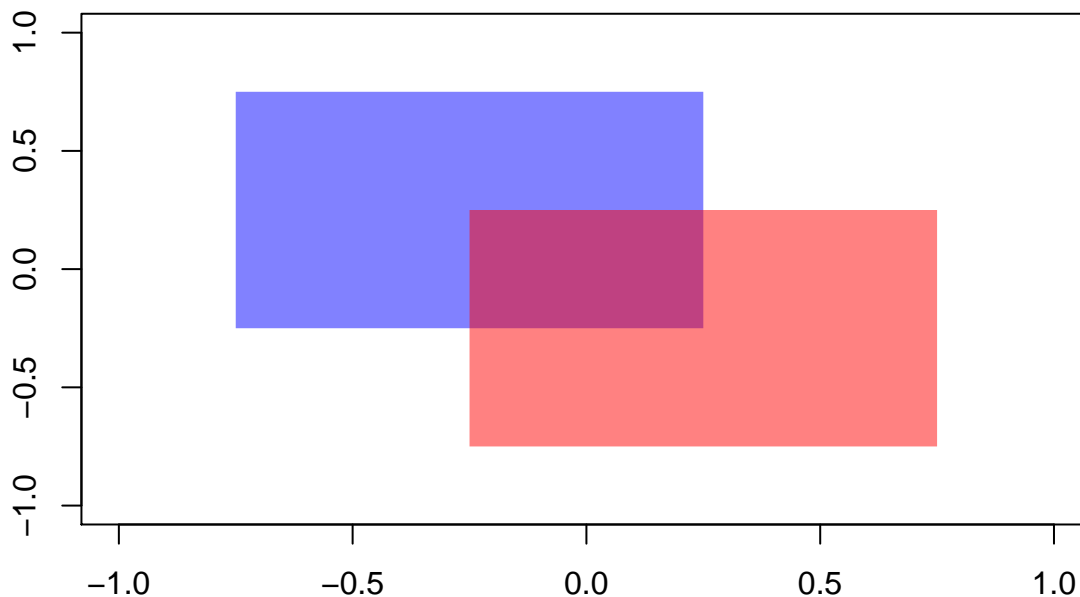
```

#example
makeTransparent = function(..., alpha=0.5) {
  if(alpha<0 | alpha>1) stop("alpha must be between 0 and 1")
  alpha = floor(255*alpha)
  newColor = col2rgb(col=unlist(list(...)), alpha=FALSE)
  .makeTransparent = function(col, alpha) {
    rgb(red=col[1], green=col[2], blue=col[3], alpha=alpha, maxColorValue=255)
  }
  newColor = apply(newColor, 2, .makeTransparent, alpha=alpha)
  return(newColor)
}

par(new=FALSE)
plot(NULL,
      xlim=c(-1, 1),
      ylim=c(-1, 1),
      xlab="",
      ylab=""
)

polygon(x=c(seq(-0.75, 0.25, length.out=100), seq(0.25, -0.75, length.out=100)),
        y=c(rep(-0.25, 100), rep(0.75, 100)), border=NA, col=makeTransparent('blue',alpha=0.5))
polygon(x=c(seq(-0.25, 0.75, length.out=100), seq(0.75, -0.25, length.out=100)),
        y=c(rep(-0.75, 100), rep(0.25, 100)), border=NA, col=makeTransparent('red',alpha=0.5))

```



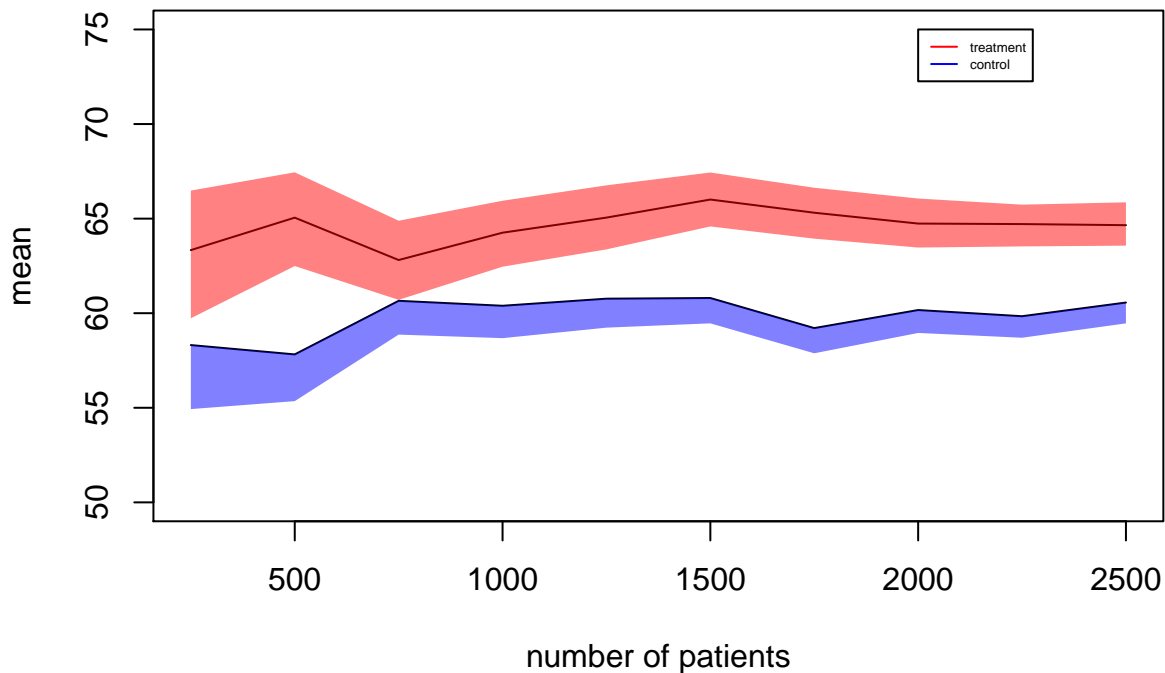
```

#make the plot
makeTransparent = function(..., alpha=0.5) {
  if(alpha<0 | alpha>1) stop("alpha must be between 0 and 1")
  alpha = floor(255*alpha)
  newColor = col2rgb(col=unlist(list(...)), alpha=FALSE)
  .makeTransparent = function(col, alpha) {
    rgb(red=col[1], green=col[2], blue=col[3], alpha=alpha, maxColorValue=255)
  }
  newColor = apply(newColor, 2, .makeTransparent, alpha=alpha)
  return(newColor)
}
plot( x=seq(250,2500,250),y=t_mean,type="l",xlab="number of patients",ylab="mean", xlim=c(250,2500),ylim=c(50,75))
polygon(x=c(seq(250,2500,250),seq(2500,250,-250)),y=c(t_lw,rev(t_up)), border=NA, col=makeTransparent('red',alpha=0.5))

lines(x=seq(250,2500,250),y=c_mean)
polygon(x=c(seq(250,2500,250),seq(2500,250,-250)),y=c(c_lw,rev(c_mean)), border=NA, col=makeTransparent('blue',alpha=0.5))

legend(2000,75,c("treatment","control"),lty=c(1,1,1),lwd=c(1,1,1),col=c("red","blue"), cex=0.45)

```



Question 4

15 points

Programming with classes. The following function will generate random patient information.

```

makePatient <- function() {
  vowel <- grep("[aeiou]", letters)
  cons <- grep("[^aeiou]", letters)
  name <- paste(sample(LETTERS[cons], 1), sample(letters[vowel], 1), sample(letters[cons], 1), sep='')
  gender <- factor(sample(0:1, 1), levels=0:1, labels=c('female','male'))
  dob <- as.Date(sample(7500, 1), origin="1970-01-01")
}

```

```

n <- sample(6, 1)
doa <- as.Date(sample(1500, n), origin="2010-01-01")
pulse <- round(rnorm(n, 80, 10))
temp <- round(rnorm(n, 98.4, 0.3), 2)
fluid <- round(runif(n), 2)
list(name, gender, dob, doa, pulse,temp, fluid)
}

```

1. Create an S3 class `medicalRecord` for objects that are a list with the named elements `name`, `gender`, `date_of_birth`, `date_of_admission`, `pulse`, `temperature`, `fluid_intake`. Note that an individual patient may have multiple measurements for some measurements. Set the RNG seed to 8 and create a medical record by taking the output of `makePatient`. Print the medical record, and print the class of the medical record. (5 points)

```

makePatient <- function() {
  vowel <- grep("[aeiou]", letters)
  cons <- grep("[^aeiou]", letters)
  name <- paste(sample(LETTERS[cons], 1), sample(letters[vowel], 1), sample(letters[cons], 1), sep='')
  gender <- factor(sample(0:1, 1), levels=0:1, labels=c('female','male'))
  dob <- as.Date(sample(7500, 1), origin="1970-01-01")
  n <- sample(6, 1)
  doa <- as.Date(sample(1500, n), origin="2010-01-01")
  pulse <- round(rnorm(n, 80, 10))
  temp <- round(rnorm(n, 98.4, 0.3), 2)
  fluid <- round(runif(n), 2)
  list(name=name, gender=gender, date_of_birth=dob, date_of_admission=doa, pulse=pulse,temperature=temp)
}

set.seed(8)
record1 <- makePatient()
class(record1) <- "medicalRecord"
print (record1)

```

```

## $name
## [1] "Mev"
##
## $gender
## [1] male
## Levels: female male
##
## $date_of_birth
## [1] "1976-08-09"
##
## $date_of_admission
## [1] "2011-03-14" "2013-10-30" "2013-02-27" "2012-08-23" "2011-11-16"
##
## $pulse
## [1] 67 81 95 74 81
##
## $temperature
## [1] 98.33 98.16 99.00 98.49 98.67
##
## $fluid_intake

```

```
## [1] 0.62 0.93 0.18 0.39 0.34
##
## attr(,"class")
## [1] "medicalRecord"
```

```
class(record1)
```

```
## [1] "medicalRecord"
```

2. Write a `medicalRecord` method for the generic function `mean`, which returns averages for pulse, temperature and fluids. Also write a `medicalRecord` method for `print`, which employs some nice formatting, perhaps arranging measurements by date, and `plot`, that generates a composite plot of measurements over time. Call each function for the medical record created in part 1. (5 points)

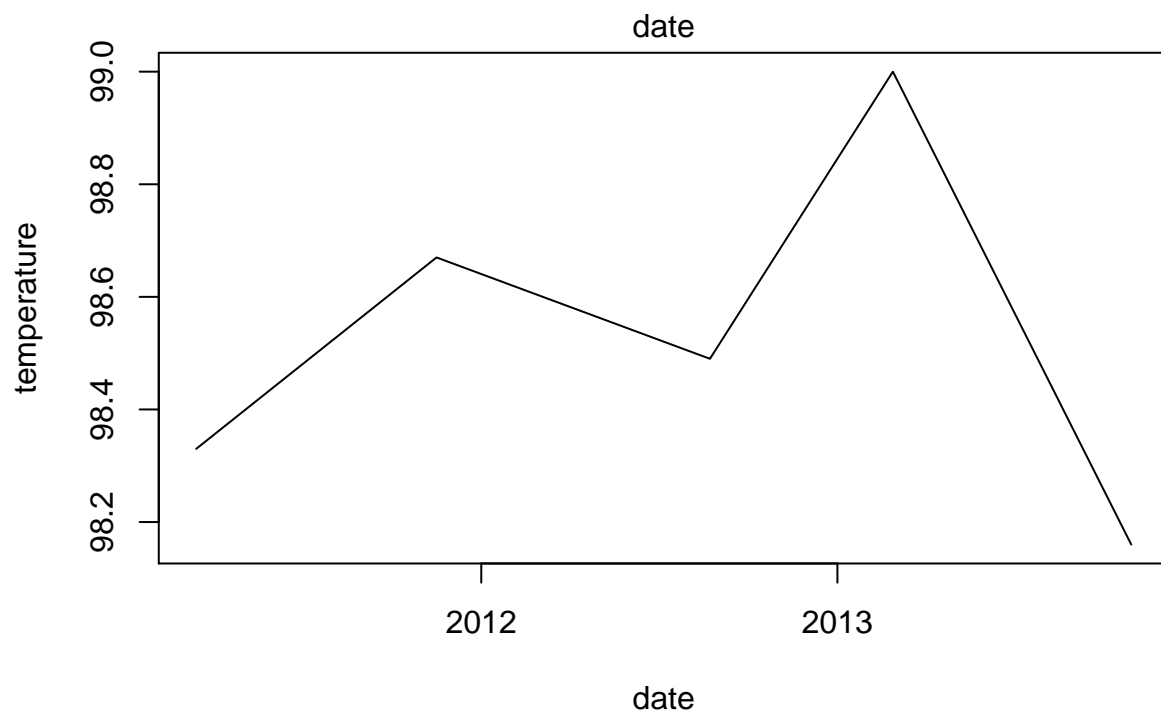
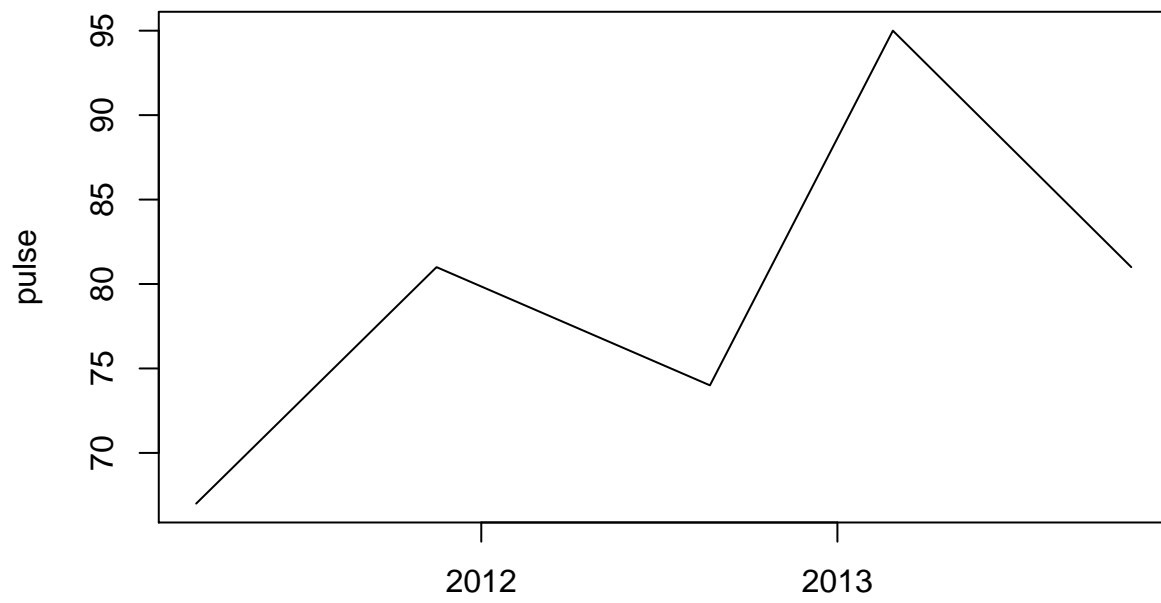
```
mean.medicalRecord<-function(x){
  list( mean(x$pulse),mean(x$temperature), mean(x$fluid) )
}
mean(record1)
```

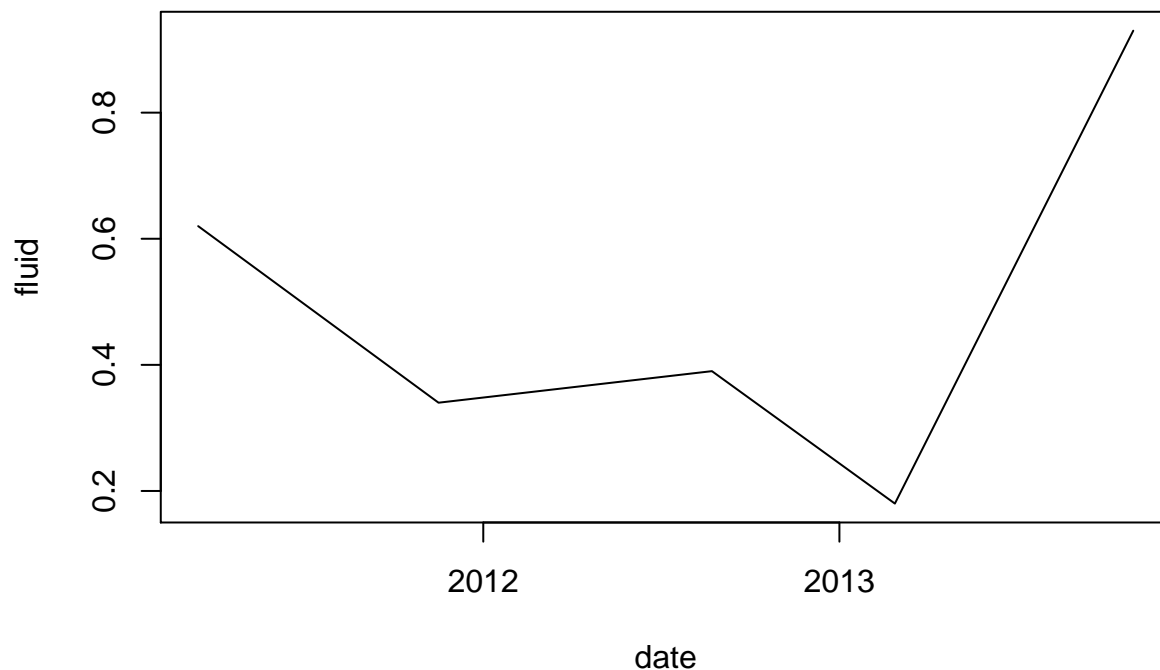
```
## [[1]]
## [1] 79.6
##
## [[2]]
## [1] 98.53
##
## [[3]]
## [1] 0.492
```

```
print.medicalRecord<-function(x){
  res <- data.frame(doa=x$date_of_admission, name=x$name,pulse=x$pulse,
                    temp=x$temperature, fluid=x$fluid_intake)
  res <- res[order(res$doa),]
  print(res)
}
print(record1)
```

```
##          doa name pulse  temp fluid
## 1 2011-03-14  Mev   67 98.33  0.62
## 5 2011-11-16  Mev   81 98.67  0.34
## 4 2012-08-23  Mev   74 98.49  0.39
## 3 2013-02-27  Mev   95 99.00  0.18
## 2 2013-10-30  Mev   81 98.16  0.93
```

```
plot.medicalRecord<-function(x){
  res <- data.frame(doa=x$date_of_admission, pulse=x$pulse,
                    temp=x$temperature, fluid=x$fluid_intake)
  res <- res[order(res$doa),]
  plot(x=res$doa,y=res$pulse,type="l",xlab="date",ylab="pulse")
  plot(x=res$doa,y=res$temp,type="l",xlab="date",ylab="temperature")
  plot(x=res$doa,y=res$fluid,type="l",xlab="date",ylab="fluid")
}
plot(record1)
```





3. Create a further class for a cohort (group) of patients, and write methods for `mean` and `print` which, when applied to a cohort, apply `mean` or `print` to each patient contained in the cohort. Hint: think of this as a “container” for patients. Reset the RNG seed to 8 and create a cohort of ten patients, then show the output for `mean` and `print`. (5 points)

```
set.seed(8)
record2 <- lapply(seq(10), function(x){makePatient()})
class(record2) <- "cohort"

mean.cohort <- function(x){
  for(i in x){
    class(i) = "medicalRecord"
    print(mean(i))
  }
}

mean(record2)
```

```
## [[1]]
## [1] 79.6
##
## [[2]]
## [1] 98.53
##
## [[3]]
## [1] 0.492
##
## [[1]]
## [1] 78
##
## [[2]]
```

```

## [1] 98.495
##
## [[3]]
## [1] 0.245
##
## [[1]]
## [1] 81.5
##
## [[2]]
## [1] 98.44
##
## [[3]]
## [1] 0.4033333
##
## [[1]]
## [1] 78
##
## [[2]]
## [1] 98.6
##
## [[3]]
## [1] 0.65
##
## [[1]]
## [1] 88.33333
##
## [[2]]
## [1] 98.05
##
## [[3]]
## [1] 0.5866667
##
## [[1]]
## [1] 83.5
##
## [[2]]
## [1] 98.45
##
## [[3]]
## [1] 0.4525
##
## [[1]]
## [1] 83
##
## [[2]]
## [1] 98.01
##
## [[3]]
## [1] 0.97
##
## [[1]]
## [1] 77.5
##
## [[2]]

```

```
## [1] 98.14833
##
## [[3]]
## [1] 0.3366667
##
## [[1]]
## [1] 77
##
## [[2]]
## [1] 98.83
##
## [[3]]
## [1] 0.445
##
## [[1]]
## [1] 79.33333
##
## [[2]]
## [1] 98.3
##
## [[3]]
## [1] 0.6583333
```

```
print.cohort <- function(x){
  for(i in x){
    class(i) = "medicalRecord"
    print(i)
  }
}

print(record2)
```

```
##          doa name pulse  temp fluid
## 1 2011-03-14  Mev    67 98.33  0.62
## 5 2011-11-16  Mev    81 98.67  0.34
## 4 2012-08-23  Mev    74 98.49  0.39
## 3 2013-02-27  Mev    95 99.00  0.18
## 2 2013-10-30  Mev    81 98.16  0.93
##          doa name pulse  temp fluid
## 1 2012-01-16  Yul    76 98.92  0.14
## 2 2013-08-07  Yul    80 98.07  0.35
##          doa name pulse  temp fluid
## 6 2010-03-21  Zet    79 98.58  0.22
## 5 2010-04-01  Zet    73 98.32  0.61
## 4 2012-08-29  Zet    88 98.47  0.59
## 3 2013-06-01  Zet    84 98.22  0.25
## 1 2013-11-03  Zet    72 98.54  0.03
## 2 2014-02-05  Zet    93 98.51  0.72
##          doa name pulse  temp fluid
## 1 2011-06-22  Qih    78 98.6   0.65
##          doa name pulse  temp fluid
## 3 2010-04-12  Wut    76 98.05  0.65
## 1 2011-02-16  Wut    93 98.26  0.97
## 2 2012-04-12  Wut    96 97.84  0.14
```

##		doa	name	pulse	temp	fluid
## 4	2010-03-10	Juy		81	99.11	0.66
## 1	2010-03-25	Juy		90	98.58	0.26
## 3	2010-04-18	Juy		75	98.58	0.60
## 2	2010-06-10	Juy		88	97.53	0.29
##		doa	name	pulse	temp	fluid
## 1	2010-03-12	God		83	98.01	0.97
##		doa	name	pulse	temp	fluid
## 5	2011-04-07	Fut		80	97.87	0.36
## 4	2011-04-14	Fut		83	97.91	0.00
## 2	2011-08-16	Fut		66	98.49	0.13
## 1	2013-03-15	Fut		74	98.38	0.31
## 6	2013-06-20	Fut		74	98.41	0.49
## 3	2013-11-12	Fut		88	97.83	0.73
##		doa	name	pulse	temp	fluid
## 1	2010-10-30	Pet		85	98.84	0.60
## 2	2012-05-10	Pet		69	98.82	0.29
##		doa	name	pulse	temp	fluid
## 4	2010-01-28	Yed		63	97.95	0.94
## 3	2010-03-06	Yed		81	98.45	0.67
## 1	2010-07-10	Yed		98	98.65	0.79
## 6	2010-08-27	Yed		66	97.68	0.36
## 5	2011-06-18	Yed		83	98.00	0.69
## 2	2013-01-06	Yed		85	99.07	0.50