Homework 4

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Problem 1

a) Let $d_1, d_2, ..., d_n$ be the differences between 25 pairs with and Δ be the median of d_i.
$H_0 : \Delta \geq 0$
$H_1 : \Delta < 0$

$n * p(1-p) \geq 5$ so I will apply normal-approximation to perform the one-sided sign test.
Let C be the number of negative differences, ignoring the zero differences; n* be the number of non-zero differences.
Now, C = 14 and n* = 24

The test statistics is:
$\frac{n^*}{2} + \frac{1}{2} + z_{1-\alpha}\sqrt{\frac{n^*}{4}} = 16.53 >$ C
p-value $= 1 - \Phi(\frac{C - \frac{n^*}{2} - \frac{1}{2}}{\sqrt{\frac{n^*}{4}}}) = 0.27$

Therefore, we fail to reject the null hypothesis. We do not have significant ($\alpha = 0.05$) evidence to support that the median sugar readings was less than 120.

b) H_0 : The median difference between blood sugar samples and 120 is equal to or greater than zero
H_1 : The median difference between blood sugar samples and 120 is less than zero

In order to perform the Wilcoxon Signed-Rank Test (one-sided), I calculated the absolute differences between samples and 120 and their rank as follows.

```r
bs = bs |>
  filter(sample != 120) |> # exclude difference = 0
  group_by(sample) |>
  mutate(
    d = sample - 120,
    abs_d = abs(d), # absolute differences
    positive_d = ifelse(d > 0, 1, 0),
    negative_d = ifelse(d < 0, 1, 0),
    same_n = n() # count numbers of same blood sugar samples
  ) |>
  ungroup() |>
  arrange(abs_d) |>
  mutate(
    rank = rank(abs_d) # assign average rank based on absolute differences
  ) |>
  print()
```

```
## # A tibble: 24 x 7
##    sample     d abs_d positive_d negative_d same_n  rank
##     <dbl> <dbl> <dbl>      <dbl>      <dbl>  <int> <dbl>
##  1    121     1     1          1          0      1   1
##  2    118    -2     2          0          1      4   4
##  3    118    -2     2          0          1      4   4
##  4    118    -2     2          0          1      4   4
##  5    122     2     2          1          0      1   4
##  6    118    -2     2          0          1      4   4
##  7    123     3     3          1          0      3   8.5
##  8    117    -3     3          0          1      1   8.5
##  9    123     3     3          1          0      3   8.5
## 10    123     3     3          1          0      3   8.5
## # i 14 more rows
```

Let R be the rank sum for negative differences.

R = 187.5
Since there are ties, the test statistics T is:
$T = \frac{|R - \frac{n^*(n^*+1)}{4}| - \frac{1}{2}}{\sqrt{(\frac{n^*(n^*+1)(2n^*+1)}{24} - \frac{\sum_{i=1}^{g}(t_i^3 - t_i)}{48})}} = 1.08 \sim \mathrm{N}(0, 1)$ under H_0
p-value $= [1 - \Phi(T)] = 0.14$
Therefore, we failed to reject the null hypothesis and cannot conclude that there is a significant ($\alpha = 0.05$) evidence that median blood sugar reading was less than 120.

Problem 2

a)

```
# exclude homo sapiens
df_brain_nonh = df_brain |>
  filter(species != "Homo sapiens")

# fit a regression model for the nonhuman data
reg_nonh = lm(glia_neuron_ratio ~ ln_brain_mass, df_brain_nonh)

reg_nonh |>
  broom::tidy() |>
  mutate_at(2:5, round, 3) |>
  mutate(
    p.value = ifelse(p.value < 0.001, "< 0.001", p.value)
  ) |>
  knitr::kable()
```

term	estimate	std.error	statistic	p.value
(Intercept)	0.164	0.160	1.024	0.322
ln_brain_mass	0.181	0.036	5.026	< 0.001

b)

```r
# prediction intervals (95%)
predict(
  reg_nonh,
  newdata = tibble(
    ln_brain_mass = df_brain |>
      filter(species == "Homo sapiens") |>
      pull(ln_brain_mass)
  ),
  interval = "prediction", level = 0.95
) |>
  round(3)
```

```
##     fit   lwr   upr
## 1 1.471 1.036 1.907
```

The predicted glia-neuron ratio for humans given the brain mass using the nonhuman primate relationship is 1.471.

c)

```r
# prediction intervals (95%)
predict(
  reg_nonh,
  newdata = tibble(
    ln_brain_mass = df_brain |>
      filter(species == "Homo sapiens") |>
      pull(ln_brain_mass)
  ),
  interval = "confidence", level = 0.95
) |>
  round(3)
```

```
##     fit  lwr   upr
## 1 1.471 1.23 1.713
```

The 95% prediction interval for the predicted human glia-neuron ratio given the brain mass is 1.036 - 1.907, and the 95% confidence interval is 1.230 - 1.713.
I would use prediction interval rather than confidence interval when it comes to prediction because the prediction interval is more conservative by accounting for both the uncertainty of estimating a value and the random variability of the sample.

d) Given the output in part (b), the 95% prediction interval is 1.036 - 1.907. The sample observation of human glia-neuron ratio is 1.65, which is within the range of the 95% prediction interval. Thus, using the regression model for nonhuman data, we can say that the human brain does not have an excessive glia-neuron ratio for its mass compared with other primates.

e) Because no other primates have brain mass as big as human, the regression model (based on primates' data) may not be able to accurately predict the `glia_neuron_ratio` with large `ln_brain_mass`.

Problem 3

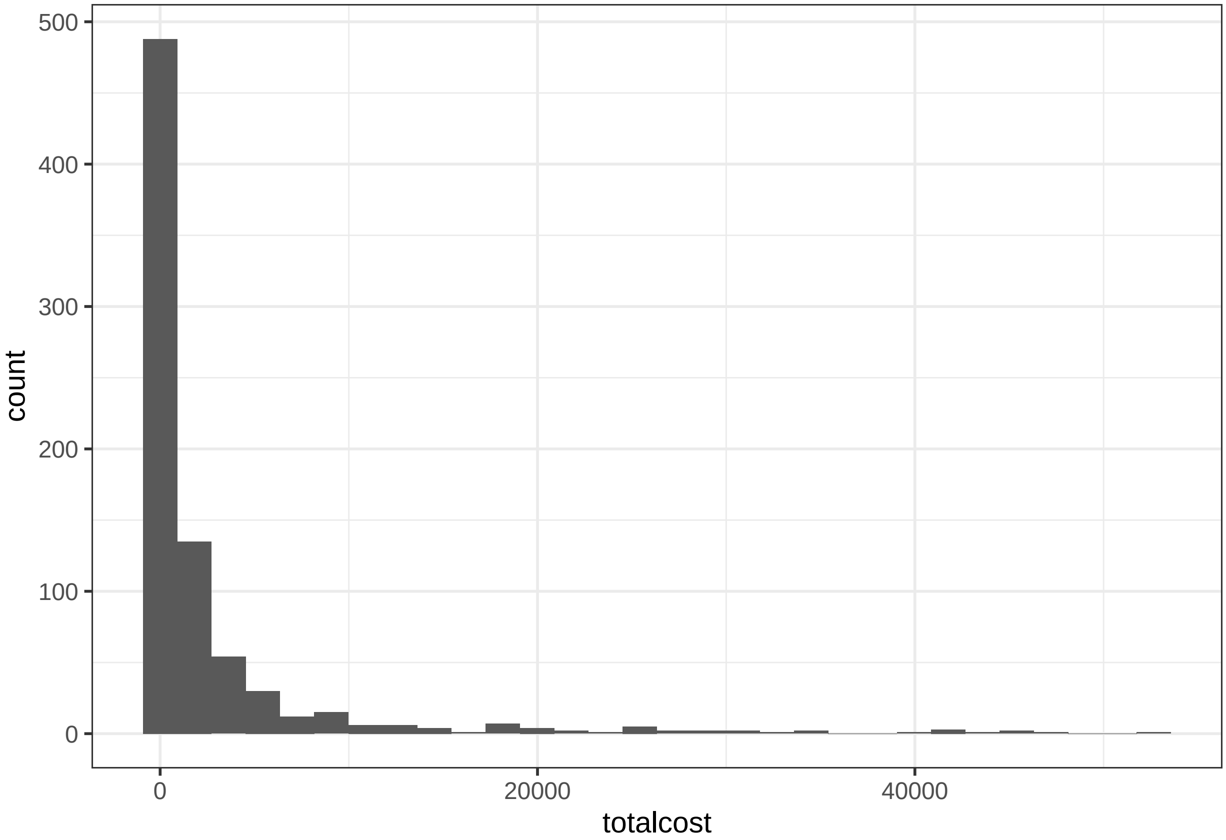
a) The data set consists of 10 variables and 788 observations.
The main outcome in this case is `totalcost` and the main predictor is `e_rvisits`. Other important covariates include `age`, `gender`, `complications`, and `duration`. (It is not specified but I will treat gender 0 as male, and 1 as female)

The descriptive statistics for all variables of interest is as follows.

Characteristic	**N = 788**[1]
Total cost (USD)	2,800.0 / 507.2 (6,690.3)
ER visits	3.4 / 3.0 (2.6)
Age	58.7 / 60.0 (6.8)
Female	180 (23%)
No. of complications	
0	745 (95%)
1	42 (5.3%)
3	1 (0.1%)
Duration of treatment condition (days)	164.0 / 165.5 (120.9)

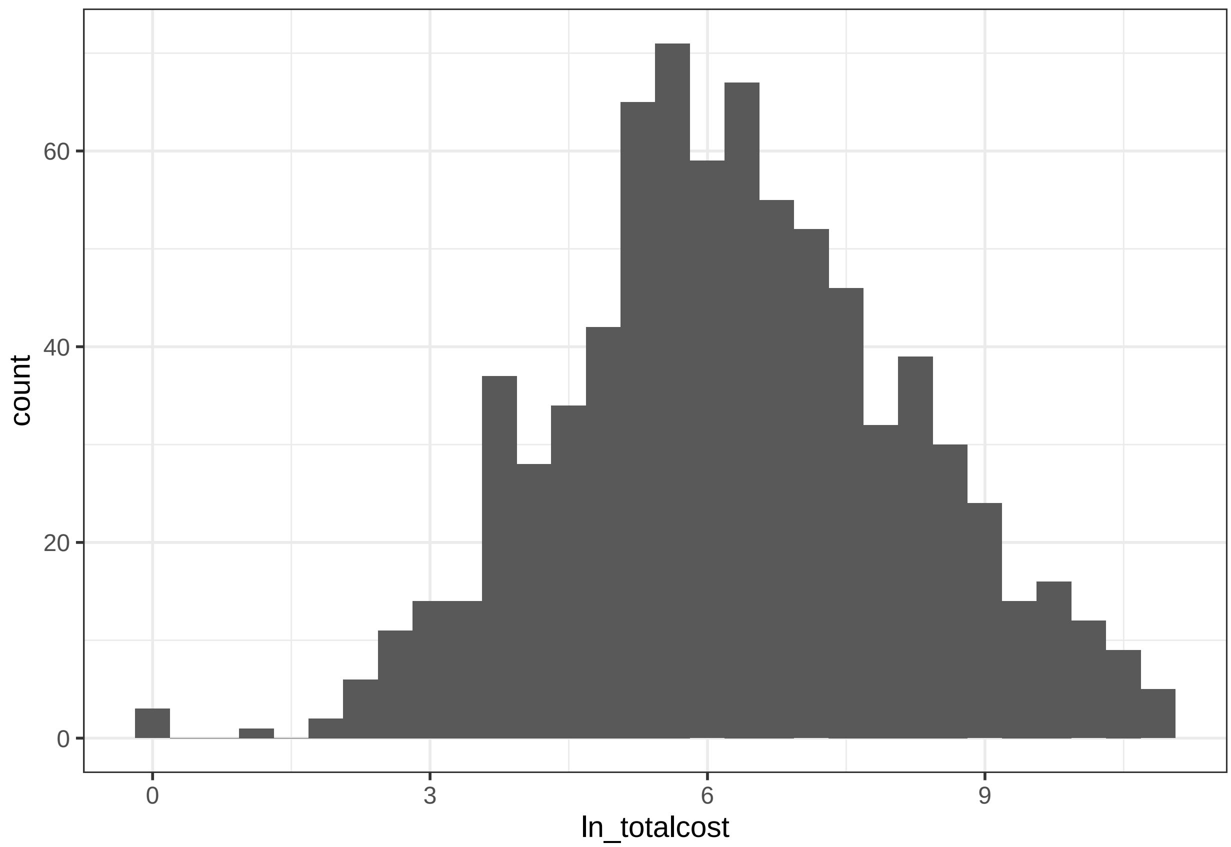
[1] Mean / Median (SD); n (%)

b)



As shown in the histogram, the distribution for variable `totalcost` is right-skewed.

I will log-transform the values of "`totalcost` + 1" (add constant term 1 to avoid $-\infty$). Now, the distribution of `ln_totalcost` is closer to the normal distribution.



c)

```
# create a new variable comp_bin (0: no complications, 1: otherwise)
df_hd = df_hd |>
  mutate(
    comp_bin = ifelse(complications == 0, 0, 1)
  )
```

d)

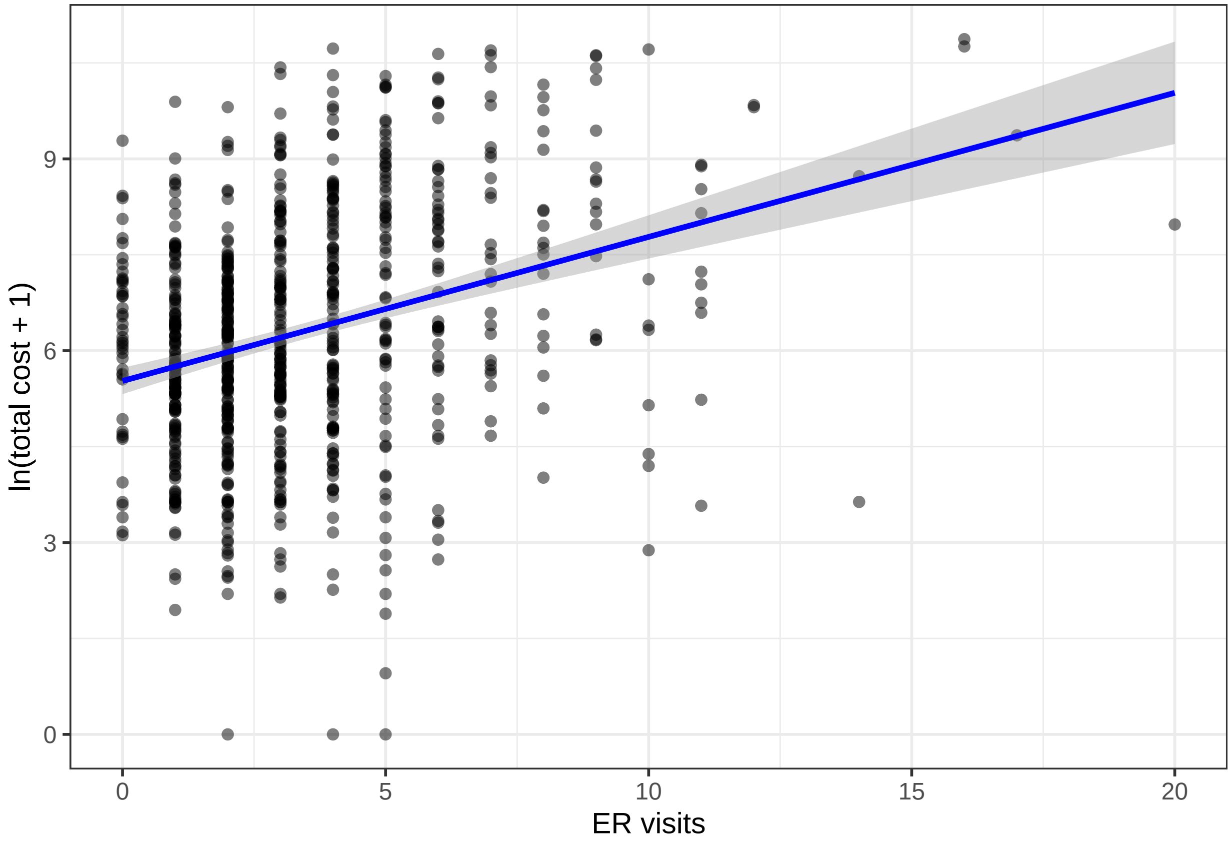
```
df_hd = df_hd |>
  mutate(
    ln_totalcost = log(totalcost + 1)
  )

# simple linear regression between ln_totalcost and e_rvisits
reg_cost_slr = lm(ln_totalcost ~ e_rvisits, data = df_hd)

reg_cost_slr |>
  broom::tidy() |>
  mutate_at(2:5, round, 3) |>
  mutate(
    p.value = ifelse(p.value < 0.001, "< 0.001", p.value)
  ) |>
  knitr::kable()
```

term	estimate	std.error	statistic	p.value
(Intercept)	5.527	0.105	52.584	< 0.001
e_rvisits	0.225	0.024	9.264	< 0.001

```
# 95% CI for model parameter e_rvisits
confint(reg_cost_slr, "e_rvisits")
```

```
##                 2.5 %    97.5 %
## e_rvisits 0.1775544 0.2730293
```

p-value for the slope ($\beta_{ERvisits}$) appears to be less than 0.05. Thus, we reject the null hypothesis ($\beta_{ERvisits} = 0$) and conclude that there is a significant linear association between the `ln_totalcost` and `e_rvisits`. 95% CI for the true slope is 0.178 - 0.273. With 95% confidence, we estimate that the `ln_totalcost` increases by somewhere between 0.178 and 0.273 for each additional ER visits.

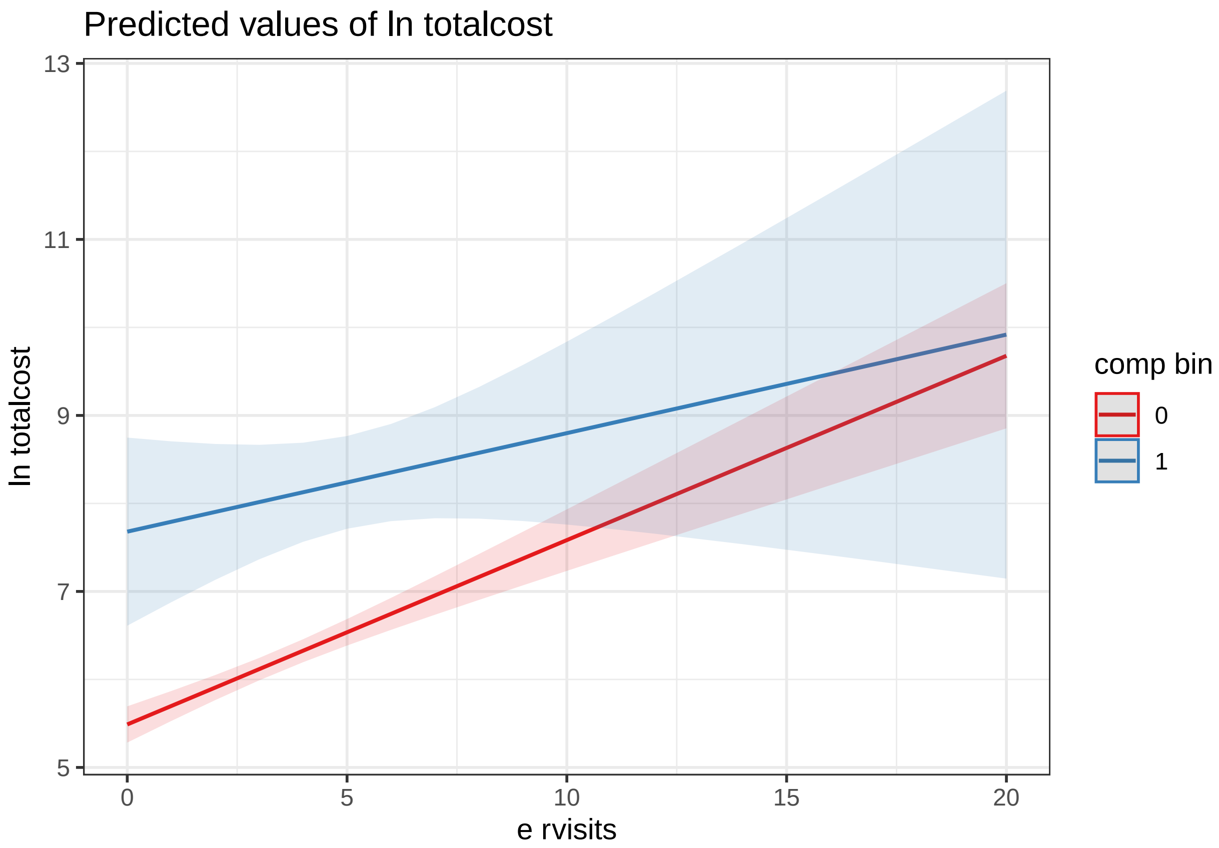


e1)

```
# multiple linear regression model (parameters: comp_bin, e_rvisits)
# assess effect modification
reg_cost_mlr1 = lm(ln_totalcost ~ e_rvisits * comp_bin, data = df_hd)

reg_cost_mlr1 |>
  broom::tidy() |>
  mutate_at(2:5, round, 3) |>
  mutate(
    p.value = ifelse(p.value < 0.001, "< 0.001", p.value)
  ) |>
  knitr::kable()
```

term	estimate	std.error	statistic	p.value
(Intercept)	5.488	0.105	52.271	< 0.001
e_rvisits	0.209	0.025	8.412	< 0.001
comp_bin	2.191	0.554	3.951	< 0.001
e_rvisits:comp_bin	-0.098	0.096	-1.013	0.311

```
# visualize the interaction
plot_model(reg_cost_mlr1, type = "int")
```



The regression coefficient associated with the interaction term `e_rvisits:comp_bin` is not statistically significant. Thus, it indicates that `comp_bin` is not an effect modifier of the relationship between `ln_totalcost` and `e_rvisits`.

e2)

```
# multiple linear regression model (parameters: comp_bin, e_rvisits)
# assess confounder
# unadjusted MLR
reg_cost_mlr2 = lm(ln_totalcost ~ e_rvisits, data = df_hd)
```

```r
reg_cost_mlr2 |>
  broom::tidy() |>
  mutate_at(2:5, round, 3) |>
  mutate(
    p.value = ifelse(p.value < 0.001, "< 0.001", p.value)
  ) |>
  knitr::kable()
```

term	estimate	std.error	statistic	p.value
(Intercept)	5.527	0.105	52.584	< 0.001
e_rvisits	0.225	0.024	9.264	< 0.001

```r
# add comp_bin
reg_cost_mlr3 = lm(ln_totalcost ~ e_rvisits + comp_bin, data = df_hd)

reg_cost_mlr3 |>
  broom::tidy() |>
  mutate_at(2:5, round, 3) |>
  mutate(
    p.value = ifelse(p.value < 0.001, "< 0.001", p.value)
  ) |>
  knitr::kable()
```

term	estimate	std.error	statistic	p.value
(Intercept)	5.510	0.103	53.606	< 0.001
e_rvisits	0.203	0.024	8.437	< 0.001
comp_bin	1.706	0.279	6.111	< 0.001

After adding `comp_bin` to the model, the change of the coefficient of `e_rvisits` was observed (-10.84%). By the rule of thumb, we can say that `comp_bin` is a confounder of the relationship between `ln_totalcost` and `e_rvisits`.

e3) Given that `comp_bin` is a potential confounder between `ln_totalcost` and `e_rvisits`, I would include this in the model so that the model can account for the impact of the confounder on the outcome.

f1)

```r
# multiple linear regression model (parameters: comp_bin, e_rvisits)
# assess effect modification
reg_cost_mlr4 = lm(ln_totalcost ~ e_rvisits + comp_bin + age + gender + duration, data = df_hd)

reg_cost_mlr4 |>
  broom::tidy() |>
  mutate_at(2:5, round, 3) |>
  mutate(
    p.value = ifelse(p.value < 0.001, "< 0.001", p.value)
  ) |>
  knitr::kable()
```

term	estimate	std.error	statistic	p.value
(Intercept)	5.940	0.510	11.639	< 0.001
e_rvisits	0.175	0.023	7.735	< 0.001
comp_bin	1.504	0.258	5.820	< 0.001
age	-0.021	0.009	-2.380	0.018
gender	-0.207	0.139	-1.491	0.136
duration	0.006	0.000	11.691	< 0.001

Statistically significant linear associations were observed between the outcome and the covariates except for `gender`. Holding all other variables constant, `ln_totalcost` increases by 0.175 for every unit change in `e_rvisits`.

f2) I would use the MLR model (from f1) because ER visits is unlikely to be a single factor that has an impact on the total cost. We need to consider other factors such as age, gender, treatment duration, etc as well.