A correlation analysis of clinical variables of TCGA-KIRC patients

This project contains a pipeline of clinical analysis of the Cancer Genome Atlas Kidney Renal Clear Cell Carcinoma (TCGA-KIRC) data of patients, from Genomic Data Commons Data Portal and cBioPortal.

Previously, we presented an exploratory preprocessing analysis. In this section, Chi-squared test is applied to compare two or more proportions of categorical variables and T-student test to compare the means of numeric ones regardind the levels of 'Overall_Survival_Status'. The Hypoteis test is performed and p-value indicates the strength of evidence in supportting the null hypothesis.

```
# Set the packages of interest
packages = c("tidyverse","skimr","finalfit","rstatix", "ggpubr","GGally", "plotly")

# if a package is installed, it will be loaded
# otherwise, the missing package(s) will be installed and loaded
package.check <- lapply(packages, FUN = function(x) {
   if (!require(x, character.only = TRUE)) {
     install.packages(x, dependencies = TRUE)
     library(x, character.only = TRUE)
   }
})

suppressMessages(library("tidyverse"))
rm(packages)
setwd(".")</pre>
```

1. Importing data

```
kirc_clin <- read_csv("data/kirc_clin.csv")</pre>
```

2. Taming data

```
kirc_clin <- kirc_clin %>%
 mutate_if(is.character, as.factor) %>%
 mutate(patient_id = as.character(patient_id),
        age = as.integer(age),
        year_diagnose = as.integer(year_diagnose))
# check
glimpse(kirc_clin)
## Rows: 537
## Columns: 29
## $ patient_id
                      <chr> "TCGA-3Z-A93Z", "TCGA-6D-AA2E", "TCGA-A3-3306",...
## $ age
                      <int> 69, 68, 67, 66, 77, 57, 59, 57, 67, 70, 52, 51,...
## $ metastasis_stg
                      ## $ lymph_stg
                      <fct> NO, NX, NO, NO, NO, NX, NO, NX, NO, NX, NX, NX, ...
```

```
## $ neoplasm stg
                        <fct> Stage I, Stage I, Stage III, Stage III...
                        <fct> T1, T1, T1, T3, T3, T1, T1, T2, T2, T1, T1, T1,...
## $ tumor_stg
## $ disease free mth
                        <dbl> 12.65, 11.89, 36.79, 47.17, 0.53, NA, NA, 49.05...
## $ disease_free_stt
                        <fct> DiseaseFree, DiseaseFree, DiseaseFree, DiseaseF...
## $ ethnicity
                        <fct> not hispanic/latino, not hispanic/latino, not h...
                        <dbl> 0.2240, 0.0000, 0.2316, 0.0494, 0.0844, 0.0883,...
## $ frac_genome_alter
                        <fct> G2, G2, G3, G3, G2, G2, G3, G3, G2, G2, G1, G2,...
## $ histology grd
                        <fct> Normal, NA, NA, NA, Normal, Low, Low, NA, NA, N...
## $ hemoglobin
## $ neoadj_therapy
                        ## $ prior_cancer
                        <fct> No, No, No, Yes, No, No, No, No, No, No, No, No...
## $ year_diagnose
                        <int> 2013, 2013, 2005, 2005, 2006, 2005, 2005, 2005,...
## $ tumor_lateral
                        <fct> Right, Right, Left, Right, Right, Right, Right, ...
## $ long_dim
                        <dbl> NA, NA, 0.9, 1.0, 1.2, 1.7, 2.0, 1.7, 1.5, 1.5,...
## $ mutation_cnt
                        <dbl> NA, NA, NA, NA, 514, 56, 656, 577, 62, 537, 477...
## $ over_surv_mth
                        <dbl> 12.65, 11.89, 36.79, 47.17, 0.53, 39.13, 24.15,...
## $ over_surv_stt
                        <fct> LIVING, LIVING, LIVING, LIVING, LIVING, DECEASE...
## $ platelet
                        <fct> Normal, NA, NA, NA, Normal, NA, NA, NA, NA, NA, NA, ...
## $ race
                        <fct> Black/African.american, Black/African.american,...
                        <fct> Normal, NA, NA, NA, Normal, NA, NA, NA, NA, NA, ...
## $ serum_ca
## $ gender
                        <fct> Male, Female, Male, Male, Female, Male, Male, M...
## $ short_dim
                        <dbl> NA, NA, 0.4, 0.6, 0.4, 0.4, 0.8, 0.8, 0.3, 0.4,...
## $ second_long_dim
                        <dbl> NA, NA, 0.7, 0.8, 1.0, 1.0, 0.9, 0.8, 1.0, 1.1,...
                        <fct> OTHERS, OTHERS, A, A, A, A, A, A, A, A, A, A...
## $ tissue_site
## $ person_neoplasm_stt <fct> Tumor.Free, Tumor.Free, NA, With.Tumor, Tumor.F...
## $ wbc
                        <fct> Normal, NA, NA, NA, Normal, NA, NA, NA, NA, NA, NA,...
```

3. The dependent variable

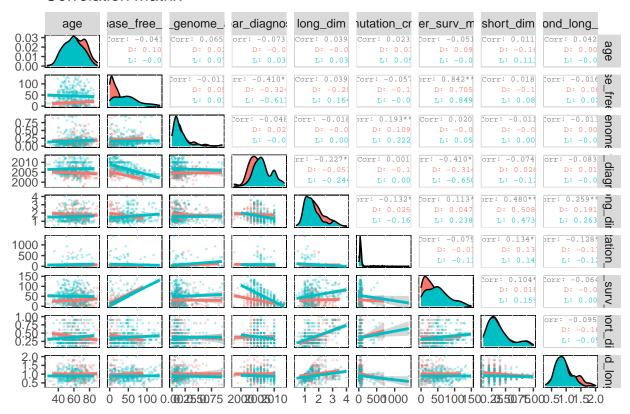
```
# Check the number of levels. If greater than 2, it thas to run a simple logistic regression presents o
table(kirc_clin$over_surv_stt, exclude = NULL)
##
## DECEASED LIVING
## 177 360
```

4. Numeric variables vs. over surv stt

Correlation matrix - graphic visualization

```
continuous = wrap("cor", size = 2, alignPercent = 0.8)),
lower = list(continuous = wrap("smooth", alpha = 0.3, size=0.2) )) +
theme(panel.background = element_rect(color = "black", size=0.5, fill="white"),
panel.grid.major = element_blank())
```

Correlation matrix



Run multiple T-tests on over_surv_stt

Transform the data into long format

```
# Put all variables in the same column except `over_surv_stt`, the grouping variable
levels(kirc_clin_numeric$over_surv_stt) <- c("DECEASED","LIVING")

# Convert to Tidyverse
kirc_clin_numeric.long <- kirc_clin_numeric %>%
    pivot_longer(-over_surv_stt, names_to = "variables", values_to = "value")
kirc_clin_numeric.long <- kirc_clin_numeric.long[!is.na(kirc_clin_numeric.long$value),]
kirc_clin_numeric.long$value.log <- log2(kirc_clin_numeric.long$value+1)

# OR
# kirc_clin_numeric.long <- kirc_clin_numeric %>%
# gather(key = 'variables', value = 'value', -over_surv_stt, na.rm = TRUE) %>%
# mutate(value.log = log2(kirc_clin_numeric.long$value+1))

kirc_clin_numeric.long %>% sample_n(6) %>% knitr::kable(.)
```

over_surv_stt	variables	value	value.log
DECEASED	long_dim	1.7	1.4329594

over_surv_stt	variables	value	value.log
LIVING	year_diagnose	2007.0	10.9715436
DECEASED	$second_long_dim$	1.5	1.3219281
DECEASED	year_diagnose	2002.0	10.9679467
LIVING	$\operatorname{short}_{\operatorname{\underline{-}dim}}$	0.3	0.3785116
LIVING	$\operatorname{mutation_cnt}$	17.0	4.1699250

Group the data by variables and compare over_surv_stt groups

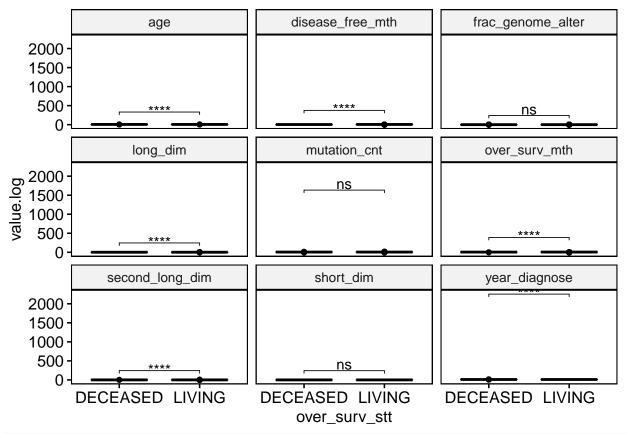
Adjust the p-values and add significance levels

```
stat.test <- kirc_clin_numeric.long %>%
  group_by(variables) %>%
  t_test(value ~ over_surv_stt) %>%
  adjust_pvalue(method = "BH") %>%
  add_significance()
stat.test %>% knitr::kable(.)
```

variables .y.	group1 group2 n1	n2	statistic	df	p	p.adj	p.adj.signif
age value	DECEASIBIIVING177	360	4.8869626	348.1670	1.60e-	0.000003	5****
					06		
disease_free_mthalue	DECEASEDVING 78	360	-	191.6452	0.00e + 0	00.000000	0****
			10.9719698	3			
frac_genome_altendue	DECEASEDVING175	353	1.1960301	343.6013	2.33e-	0.262125	$0 \mathrm{ns}$
					01		
long_dim value	DECEASEDVING173	329	4.1297313	363.4507	4.51e-	0.000081	2****
					05		
mutation_cnt value	DECEASEDVING153	298	-	428.8339	6.79e-	0.087300	$0\mathrm{ns}$
			1.8305701		02		
over_surv_mth value	DECEASEDVING177	360	-	450.9227	0.00e + 0	00.000000	0****
			7.3171956				
second_long_dimalue	DECEASEDVING173	329	4.0638742	287.9183	6.23e-	0.000093	4****
					05		
short_dim value	DECEASEDVING173	329	0.4784069	344.6781	6.33e-	0.633000	$0\mathrm{ns}$
					01		
year_diagnose value	DECEASEDVING177	360	_	377.0943	0.00e + 0	00.000000	0****
			8.8979681				

```
# Create the plot on logscale
myplot <- ggboxplot(
   kirc_clin_numeric.long, x = "over_surv_stt", y = "value.log",
   fill = "over_surv_stt", palette = "npg", legend = "none",
   ggtheme = theme_pubr(border = TRUE)
   ) +
   facet_wrap(~variables)

# Add statistical test p-values
# OBS: different p-values over vaule vs. log.value!!
stat.test <- stat.test %>% add_xy_position(x = "over_surv_stt")
myplot + stat_pvalue_manual(stat.test, label = "p.adj.signif")
```



```
79, 75, 86, 41, 75, 79, 68, 76, 34, 42, 74, 62, 57, 82, 60, 50, 46, 72, 48, 64, 54, 51, 51, 60, 54, 69, 52,
   46, 49, 47, 57, 49, 78, 59, 74, 75, 37, 65, 68, 37, 65, 62, 54, 61, 62, 48, 72, 40, 58, 45, 80, 69, 83, 85,
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```
# Add statitistical tests to each corresponding plot
# variables <- graphs$variables</pre>
# for(i in 1:length(variables)){
  qraph.i <- qraphs$plots[[i]] +</pre>
#
      labs(title = variables[i]) +
#
      #stat_pvalue_manual(stat.test[i, ], label = "p.adj.signif")
#
  print(graph.i)
# }
# Error in print(graph.i) : objeto 'graph.i' não encontrado
# ggplot(kirc_clin, aes(age, fill= over_surv_stt)) +
  qeom histogram(bins = 15, position = "dodge")
# t.test(kirc_clin$age ~ kirc_clin$over_surv_stt)
# ggplot(kirc_clin, aes(year_diagnose, fill= over_surv_stt)) +
   qeom histogram(bins = 15, position = "dodge")
# t.test(kirc_clin$year_diagnose ~ kirc_clin$over_surv_stt)
# ggplot(kirc_clin, aes(x=over_surv_stt, y=disease_free_mth)) +
  geom\_boxplot(width = .5) +
   qeom_jitter(width = 0.05, alpha = 0.2, color = "orange")
# t.test(kirc_clin$disease_free_mth ~ kirc_clin$over_surv_stt)
# ggplot(kirc_clin, aes(x=over_surv_stt, y=frac_genome_alter)) +
   qeom\_boxplot(width = .5) +
   geom_jitter(width = 0.05, alpha = 0.2, color = "orange")
# t.test(kirc_clin$frac_qenome_alter ~ kirc_clin$over_surv_stt)
# qqplot(kirc clin, aes(x=over surv stt, y=long dim)) +
   geom_boxplot(width = .5) +
  geom_jitter(width = 0.05, alpha = 0.2, color = "orange")
# t.test(kirc_clin$long_dim ~ kirc_clin$over_surv_stt)
# ggplot(kirc_clin, aes(x=over_surv_stt, y=mutation_cnt)) +
   geom\_boxplot(width = .5) +
    geom_jitter(width = 0.05, alpha = 0.2, color = "orange")
# t.test(kirc_clin$mutation_cnt ~ kirc_clin$over_surv_stt)
# ggplot(kirc_clin, aes(x=over_surv_stt, y=over_surv_mth)) +
   qeom\_boxplot(width = .5) +
   geom_jitter(width = 0.05, alpha = 0.2, color = "orange")
# t.test(kirc_clin$over_surv_mth ~ kirc_clin$over_surv_stt)
# qqplot(kirc_clin, aes(x=over_surv_stt, y=short_dim)) +
   geom\_boxplot(width = .5) +
  qeom\ jitter(width = 0.05,\ alpha = 0.2,\ color = "orange")
# t.test(kirc_clin$short_dim ~ kirc_clin$over_surv_stt)
# ggplot(kirc_clin, aes(x=over_surv_stt, y=second_long_dim)) +
  geom\ boxplot(width = .5) +
  geom_jitter(width = 0.05, alpha = 0.2, color = "orange")
```

t.test(kirc_clin\$second_long_dim ~ kirc_clin\$over_surv_stt)

Summary for continuous explanatory variables use a parametric or non-parametric test??

Dependent: over_surv_stt		DECEASED	LIVING	p
age	Mean (SD)	64.2 (12.0)	58.8 (11.9)	< 0.001
$disease_free_mth$	Mean (SD)	16.4 (18.2)	45.5(31.5)	< 0.001
frac_genome_alter	Mean (SD)	0.2(0.2)	0.2(0.2)	0.230
year_diagnose	Mean (SD)	2004.6(2.4)	2006.7(2.7)	< 0.001
long_dim	Mean (SD)	1.8 (0.6)	1.6(0.7)	< 0.001
mutation_cnt	Mean (SD)	60.5 (90.9)	80.7 (142.7)	0.111
$over_surv_mth$	Mean (SD)	31.6(25.1)	50.5 (33.6)	< 0.001
short_dim	Mean (SD)	0.4(0.2)	0.4(0.2)	0.631
$second_long_dim$	Mean (SD)	1.0 (0.3)	0.9(0.3)	< 0.001

```
# Correlation Matrix
# Pearson's (normal distribution) or Spearman (not-normal) correlations
corr_num <- kirc_clin %>%
        select_if(is.numeric) %>%
        drop_na()

# Check the correlation between variables to exclude the highy correlated
cor_matrix <- cor(corr_num, method = "spearman")
cor_matrix <- round(cor_matrix, 2)</pre>
cor_matrix
```

```
##
                       age disease_free_mth frac_genome_alter year_diagnose
## age
                      1.00
                                      -0.06
                                                         0.17
                                                                      -0.03
                                       1.00
                                                        -0.05
                                                                      -0.32
## disease_free_mth -0.06
                                      -0.05
                                                        1.00
                                                                      -0.04
## frac_genome_alter 0.17
## year_diagnose
                     -0.03
                                      -0.32
                                                        -0.04
                                                                       1.00
## long_dim
                      0.03
                                      0.02
                                                         0.05
                                                                      -0.29
                                      -0.03
                                                         0.23
                                                                       0.04
## mutation_cnt
                     0.26
## over_surv_mth
                     -0.02
                                      0.83
                                                        -0.02
                                                                      -0.45
                                                                      -0.19
## short_dim
                      0.06
                                       0.06
                                                        -0.03
                                      -0.02
## second_long_dim
                      0.02
                                                        -0.02
                                                                      -0.06
                     long_dim mutation_cnt over_surv_mth short_dim second_long_dim
##
## age
                         0.03
                                      0.26
                                                   -0.02
                                                              0.06
                                                                              0.02
## disease free mth
                         0.02
                                     -0.03
                                                    0.83
                                                              0.06
                                                                             -0.02
## frac_genome_alter
                         0.05
                                     0.23
                                                   -0.02
                                                             -0.03
                                                                             -0.02
```

## year_diagnose	-0.29	0.04	-0.45	-0.19	-0.06
## long_dim	1.00	-0.05	0.14	0.37	0.34
## mutation_cnt	-0.05	1.00	-0.02	0.11	-0.10
## over_surv_mth	0.14	-0.02	1.00	0.14	-0.01
## short_dim	0.37	0.11	0.14	1.00	-0.07
## second long dim	0.34	-0.10	-0.01	-0.07	1.00

5. Categorical variables vs. over_surv_stt

Tabulation and chi-square test

Summary for chategorical explanatory variables Chi-squared warnings will be generated when the expected count in any cell is less than 5.

```
## Warning in chisq.test(tumor_stg, over_surv_stt): Chi-squared approximation may
## be incorrect

## Warning in chisq.test(histology_grd, over_surv_stt): Chi-squared approximation
## warning in chisq.test(hemoglobin, over_surv_stt): Chi-squared approximation may
## be incorrect

## Warning in chisq.test(tumor_lateral, over_surv_stt): Chi-squared approximation
## may be incorrect

## Warning in chisq.test(race, over_surv_stt): Chi-squared approximation may be
## incorrect

## Warning in chisq.test(serum_ca, over_surv_stt): Chi-squared approximation may be
## incorrect

## Warning in chisq.test(serum_ca, over_surv_stt): Chi-squared approximation may be
## incorrect

## Warning in chisq.test(wbc, over_surv_stt): Chi-squared approximation may be
## incorrect

knitr::kable(table_char, row.names=FALSE, align=c("l", "l", "r", "r", "r"))
```

Dependent: over_surv	v_stt	DECEASED	LIVING	p
metastasis_stg	M0	110 (62.1)	316 (87.8)	< 0.001
	M1	64 (36.2)	15 (4.2)	
	MX	3(1.7)	27(7.5)	

N1	Dependent: over_surv_str	,	DECEASED	LIVING	p
NI		(Missing)	0 (0.0)	2 (0.6)	
NX	lymph_stg	N0	85 (48.0)	155 (43.1)	0.001
Stage I		N1	12 (6.8)	5 (1.4)	
Stage I		NX	80 (45.2)	200 (55.6)	
Stage II	neoplasm stg	Stage I	, ,	` /	< 0.001
Stage III	1 _ 0		, ,	,	
tumor_stg		_	, ,	,	
tumor_stg		_	` ′	` /	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		_	, ,	` /	
T2	tumor stg	`	` '	, ,	< 0.001
T3	_508		` ′	` /	10.001
T4			, ,	, ,	
disease_free_stt DiseaseFree Recurred/Progressed (Missing) 0 (0.0) (0			` ′	,	
Recurred/Progressed (Missing)	dispasa fron stt		` '	, ,	<0.001
ethnicity (Missing) 99 (55.9) 0 (0.0) hispanic/latino 3 (1.7) 23 (6.4) 0.017 not hispanic/latino 132 (74.6) 227 (63.1) (Missing) 42 (23.7) 110 (30.6) histology_grd G1 0 (0.0) 14 (3.9) <0.001 G2 45 (25.4) 185 (51.4) G3 74 (41.8) 133 (36.9) G4 (57.32.2) 21 (5.8) GX (1.06) 4 (1.1) (Missing) 0 (0.0) 3 (0.8) hemoglobin Elevated 3 (1.7) 2 (0.6) <0.001 Low 118 (66.7) 145 (40.3) Normal 43 (24.3) 143 (39.7) (Missing) 13 (7.3) 70 (19.4) Normal 43 (24.3) 143 (39.7) Yes 10 (5.6) 8 (2.2) prior_cancer No 153 (86.4) 306 (85.0) 0.753 Yes 24 (13.6) 54 (15.0) Left 98 (55.4) 155 (43.1) Right 79 (44.6) 204 (56.7) platelet Elevated 30 (16.9) 8 (2.2) <0.001 Low 20 (11.3) 26 (7.2) Normal 108 (61.0) 252 (70.0) (Missing) 19 (10.7) 74 (20.6) race Asian 1 (0.6) 7 (1.9) 0.032 Black/African.american 11 (6.2) 45 (1.5) White 163 (92.1) 303 (84.2) (Missing) 2 (1.1) 5 (1.4) serum_ca Elevated 9 (5.1) 1 (0.3) 0.003 (1.5) Normal 108 (61.0) 252 (70.0) (Missing) 2 (1.1) 5 (1.4) serum_ca Elevated 9 (5.1) 1 (0.3) 0.001 (Missing) 40 (22.6) 132 (36.7) gender Female 65 (36.7) 126 (35.0) 0.767 Male 112 (63.3) 234 (65.0) 1 tissue_site A 11 (6.2) 68 (18.9) <0.001 tissue_site A 11 (6.2) 68 (18.9) <0.001	disease_free_stt		, ,	,	<0.001
ethnicity hispanic/latino not hispanic/latino not hispanic/latino (Missing) 42 (23.7) 23 (6.4) 0.017 not hispanic/latino (Missing) 42 (23.7) 110 (30.6) (Missing) 42 (23.7) 110 (30.6) (Missing) 42 (23.7) 110 (30.6) (Missing) 45 (25.4) 185 (51.4) (G2 45 (25.4) 185 (51.4) (G3 74 (41.8) 133 (36.9) (G4 57 (32.2) 21 (5.8) (GX 1 (0.6) 4 (1.1) (Missing) 0 (0.0) 3 (0.8) (Missing) 0 (0.0) 3 (0.8) (Missing) (Missing) 10 (0.0) 3 (0.8) (Missing) (Missing) 13 (7.3) 70 (19.4) (Missing) (Mi		, –	, ,		
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	at land aites	` ~,	, ,	\ /	0.017
$\begin{array}{c} \text{histology_grd} & \begin{array}{c} \text{(Missing)} \\ \text{G1} \\ \text{G2} \\ \text{G2} \\ \text{A5} & (25.4) \\ \text{G3} \\ \text{G4} \\ \text{G3} \\ \text{G4} \\ \text{A1.8} \\ \text{133} & (36.9) \\ \text{G4} \\ \text{G3} \\ \text{C4} \\ \text{A57} & (32.2) \\ \text{21} & (5.8) \\ \text{GX} \\ \text{GX} \\ \text{I } & (0.6) \\ \text{A } & (1.1) \\ \text{(Missing)} \\ \text{O } & (0.0) \\ \text{3 } & (0.8) \\ \text{A} \\ \text{Normal} \\ \text{(Missing)} \\ \text{Normal} \\ \text{(Missing)} \\ \text{Normal} \\ \text{(Missing)} \\ \text{Normal} \\ \text{(Missing)} \\ (Missing)$	ethnicity		,	. ,	0.017
histology_grd G1 G2 45 (25.4) 185 (51.4) G3 74 (41.8) 133 (36.9) G4 57 (32.2) 21 (5.8) GX 1 (0.6) 4 (1.1) (Missing) 0 (0.0) 3 (0.8) hemoglobin Elevated 3 (1.7) 2 (0.6) <0.001 Low 118 (66.7) 145 (40.3) Normal (Missing) 13 (7.3) 70 (19.4) neoadj_therapy No 167 (94.4) 352 (97.8) 0.069 Yes 10 (5.6) 8 (2.2) prior_cancer No 153 (86.4) 306 (85.0) 0.753 Yes 24 (13.6) 54 (15.0) tumor_lateral Bilateral 0 (0.0) 1 (0.3) 0.023 Left 98 (55.4) 155 (43.1) Right 79 (44.6) 204 (56.7) platelet Elevated 30 (16.9) 8 (2.2) <0.001 Low 20 (11.3) 26 (7.2) Normal (Missing) 19 (10.7) 74 (20.6) race Asian 1 (0.6) 7 (1.9) 0.032 Black/African.american (Missing) 19 (10.7) 74 (20.6) race Asian 1 (0.6) 7 (1.9) 0.032 Black/African.american (Missing) 2 (1.1) 5 (1.4) serum_ca Elevated 9 (5.1) 1 (0.3) 0.001 Low 66 (37.3) 138 (38.3) Normal 62 (35.0) 89 (24.7) (Missing) 40 (22.6) 132 (36.7) gender Female 65 (36.7) 126 (35.0) 0.767 Male 11 (6.2) 68 (18.9) <0.001			, ,	, ,	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	11	` ~,	, ,	,	.0.001
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	histology_grd		` '	, ,	< 0.001
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			` ′		
$\begin{array}{c} \operatorname{GX} & 1 \ (0.6) & 4 \ (1.1) \\ (\operatorname{Missing}) & 0 \ (0.0) & 3 \ (0.8) \\ \end{array} \\ \operatorname{hemoglobin} & \operatorname{Elevated} & 3 \ (1.7) & 2 \ (0.6) & < 0.001 \\ \operatorname{Low} & 118 \ (66.7) & 145 \ (40.3) \\ \operatorname{Normal} & 43 \ (24.3) & 143 \ (39.7) \\ (\operatorname{Missing}) & 13 \ (7.3) & 70 \ (19.4) \\ \end{array} \\ \operatorname{neoadj_therapy} & \operatorname{No} & 167 \ (94.4) & 352 \ (97.8) & 0.069 \\ \operatorname{Yes} & 10 \ (5.6) & 8 \ (2.2) \\ \operatorname{prior_cancer} & \operatorname{No} & 153 \ (86.4) & 306 \ (85.0) & 0.753 \\ \operatorname{Yes} & 24 \ (13.6) & 54 \ (15.0) \\ \end{array} \\ \operatorname{tumor_lateral} & \operatorname{Bilateral} & 0 \ (0.0) & 1 \ (0.3) & 0.023 \\ \operatorname{Left} & 98 \ (55.4) & 155 \ (43.1) \\ \operatorname{Right} & 79 \ (44.6) & 204 \ (56.7) \\ \end{array} \\ \operatorname{platelet} & \operatorname{Elevated} & 30 \ (16.9) & 8 \ (2.2) & < 0.001 \\ \operatorname{Low} & 20 \ (11.3) & 26 \ (7.2) \\ \operatorname{Normal} & 108 \ (61.0) & 252 \ (70.0) \\ (\operatorname{Missing}) & 19 \ (10.7) & 74 \ (20.6) \\ \end{array} \\ \operatorname{race} & \operatorname{Asian} & 1 \ (0.6) & 7 \ (1.9) & 0.032 \\ \operatorname{Black/African.american} & 11 \ (6.2) & 45 \ (12.5) \\ \operatorname{White} & [163 \ (92.1) & 303 \ (84.2) \\ (\operatorname{Missing}) & 2 \ (1.1) & 5 \ (1.4) \\ \end{array} \\ \operatorname{serum_ca} & \operatorname{Elevated} & 9 \ (5.1) & 1 \ (0.3) & 0.001 \\ \operatorname{Low} & 66 \ (37.3) & 138 \ (38.3) \\ \operatorname{Normal} & 62 \ (35.0) & 89 \ (24.7) \\ (\operatorname{Missing}) & 40 \ (22.6) & 132 \ (36.7) \\ \end{array} \\ \operatorname{gender} & \operatorname{Female} & 65 \ (36.7) \ 126 \ (35.0) & 0.767 \\ \operatorname{Male} & 112 \ (63.3) \ 234 \ (65.0) \\ \operatorname{tissue_site} & A & 11 \ (6.2) \ 68 \ (18.9) & < 0.001 \\ \end{array}$, ,	,	
$\begin{array}{c} \text{hemoglobin} & \begin{array}{c} \text{(Missing)} \\ \text{Elevated} \\ \text{Low} \\ \text{Normal} \\ \text{(Missing)} \\ \end{array} & \begin{array}{c} 3 \ (1.7) \\ \text{2} \ (0.6) \\ \text{20.001} \\ \end{array} \\ \begin{array}{c} \text{Low} \\ \text{Normal} \\ \text{(Missing)} \\ \end{array} & \begin{array}{c} 118 \ (66.7) \\ \text{145} \ (40.3) \\ \text{143} \ (39.7) \\ \end{array} \\ \text{(Missing)} \\ \end{array} & \begin{array}{c} 13 \ (7.3) \\ \text{167} \ (94.4) \\ \text{352} \ (97.8) \\ \end{array} & \begin{array}{c} 0.069 \\ \text{Yes} \\ \end{array} & \begin{array}{c} 10 \ (5.6) \\ \text{8} \ (2.2) \\ \end{array} \\ \text{prior_cancer} \\ \end{array} & \begin{array}{c} \text{No} \\ \text{No} \\ \text{Yes} \\ \end{array} & \begin{array}{c} 10 \ (5.6) \\ \text{10} \ (5.6) \\ \end{array} & \begin{array}{c} 8 \ (2.2) \\ \text{22} \\ \end{array} \\ \text{prior_cancer} \\ \end{array} & \begin{array}{c} \text{No} \\ \text{No} \\ \text{Yes} \\ \end{array} & \begin{array}{c} 24 \ (13.6) \\ \text{54} \ (15.0) \\ \end{array} \\ \text{tumor_lateral} \\ \end{array} & \begin{array}{c} \text{Bilateral} \\ \text{Bilateral} \\ \text{Right} \\ \end{array} & \begin{array}{c} 0 \ (0.0) \\ \text{1} \ (0.3) \\ \end{array} & \begin{array}{c} 0.023 \\ \text{24} \ (13.6) \\ \end{array} \\ \text{Elevated} \\ \end{array} & \begin{array}{c} 30 \ (16.9) \\ \text{8} \ (2.2) \\ \end{array} & \begin{array}{c} < 0.001 \\ \text{Elevated} \\ \end{array} & \begin{array}{c} 30 \ (16.9) \\ \text{8} \ (2.2) \\ \end{array} & \begin{array}{c} < 0.001 \\ \text{Commal} \\ \end{array} \\ \begin{array}{c} \text{Asian} \\ \text{108} \ (61.0) \\ \end{array} & \begin{array}{c} 252 \ (70.0) \\ \text{Commal} \\ \text{Missing} \\ \end{array} & \begin{array}{c} 10 \ (0.6) \\ \text{7} \ (1.9) \\ \end{array} & \begin{array}{c} 0.032 \\ \text{Black/African.american} \\ \text{White} \\ \end{array} & \begin{array}{c} 11 \ (6.2) \\ \text{45} \ (12.5) \\ \text{Missing} \\ \end{array} & \begin{array}{c} 2 \ (1.1) \\ \text{5} \ (1.4) \\ \end{array} \\ \text{Serum_ca} & \begin{array}{c} \text{Elevated} \\ \text{Elevated} \\ \end{array} & \begin{array}{c} 9 \ (5.1) \\ \text{Missing} \\ \end{array} & \begin{array}{c} 1 \ (0.3) \\ \text{Commal} \\ \end{array} & \begin{array}{c} 0.001 \\ \text{Missing} \\ \end{array} & \begin{array}{c} 0.001 \\ \text{Missing} \\ \end{array} & \begin{array}{c} 0.001 \\ \text{Missing} \\ \end{array} & \begin{array}{c} 0.001 \\ \text{Male} \\ \end{array} & \begin{array}{c} 112 \ (63.3) \\ \end{array} & \begin{array}{c} 234 \ (65.0) \\ \text{Commal} \\ \end{array} & \begin{array}{c} 0.001 \\ \text{Commal} \\ \end{array} \\ \begin{array}{c} 0.001 \\ \text{Commal} \\ \end{array} & \begin{array}{c} 0.001 \\ \text{Commal} \\ \end{array} & \begin{array}{c} 0.001 \\ \text{Commal} \\ \end{array} \\ \begin{array}{c} 0.001 \\ \text{Commal}$, ,	, ,	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$, ,	\ /	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			0 (0.0)		
Normal	hemoglobin	Elevated	3(1.7)	2(0.6)	< 0.001
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$			118 (66.7)	145 (40.3)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Normal	43(24.3)	143 (39.7)	
Yes 10 (5.6) 8 (2.2) prior_cancer No 153 (86.4) 306 (85.0) 0.753 Yes 24 (13.6) 54 (15.0) 10.03 0.023 tumor_lateral Bilateral 0 (0.0) 1 (0.3) 0.023 Left 98 (55.4) 155 (43.1) 155 (43.1) 155 (43.1) 155 (43.1) 155 (43.1) 155 (43.1) 10.03 10.023 10.03 10.023 10.03 10.023 10.03 10.023 10.01 10.03 10.01 10.03 10.01 10.03 10.01 10.03 10.01 10.03 10.01 10.03 <td></td> <td>(Missing)</td> <td>13 (7.3)</td> <td>70 (19.4)</td> <td></td>		(Missing)	13 (7.3)	70 (19.4)	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	neoadj_therapy	No	167(94.4)	352 (97.8)	0.069
$\begin{array}{cccccccccccccccccccccccccccccccccccc$		Yes	10(5.6)	8 (2.2)	
$\begin{array}{c} \text{Yes} & 24 \ (13.6) & 54 \ (15.0) \\ \text{tumor_lateral} & \text{Bilateral} & 0 \ (0.0) & 1 \ (0.3) & 0.023 \\ \text{Left} & 98 \ (55.4) & 155 \ (43.1) \\ \text{Right} & 79 \ (44.6) & 204 \ (56.7) \\ \text{Platelet} & \text{Elevated} & 30 \ (16.9) & 8 \ (2.2) & <0.001 \\ \text{Low} & 20 \ (11.3) & 26 \ (7.2) \\ \text{Normal} & 108 \ (61.0) & 252 \ (70.0) \\ \text{(Missing)} & 19 \ (10.7) & 74 \ (20.6) \\ \text{race} & \text{Asian} & 1 \ (0.6) & 7 \ (1.9) & 0.032 \\ \text{Black/African.american} & 11 \ (6.2) & 45 \ (12.5) \\ \text{White} & 163 \ (92.1) & 303 \ (84.2) \\ \text{(Missing)} & 2 \ (1.1) & 5 \ (1.4) \\ \text{serum_ca} & \text{Elevated} & 9 \ (5.1) & 1 \ (0.3) & 0.001 \\ \text{Low} & 66 \ (37.3) & 138 \ (38.3) \\ \text{Normal} & 62 \ (35.0) & 89 \ (24.7) \\ \text{(Missing)} & 40 \ (22.6) & 132 \ (36.7) \\ \text{gender} & \text{Female} & 65 \ (36.7) & 126 \ (35.0) & 0.767 \\ \text{Male} & 112 \ (63.3) & 234 \ (65.0) \\ \text{tissue_site} & A & 11 \ (6.2) & 68 \ (18.9) & <0.001 \\ \end{array}$	prior_cancer	No	153 (86.4)	306 (85.0)	0.753
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		Yes	$24\ (13.6)$		
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	tumor lateral	Bilateral	, ,	, ,	0.023
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	_		` '	\ /	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$					
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	platelet			, ,	< 0.001
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	P		, ,	, ,	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$, ,	, ,	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$					
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	race	/	, ,	, ,	0.032
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Tacc		, ,	. ,	0.002
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$, ,	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$, ,	, ,	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	COPILM GO		, ,	, ,	0.001
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	serum_ca		, ,	. ,	0.001
$\begin{array}{cccccccccccccccccccccccccccccccccccc$, ,	, ,	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$, ,	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1	/	, ,	, ,	0.705
tissue_site A $11(6.2)$ $68(18.9)$ < 0.001	gender		, ,	, ,	0.767
			, ,	, ,	
B 112 (63 3) 191 (53 1)	tissue_site			, ,	< 0.001
2 112 (00.0) 101 (00.1)		В	112 (63.3)	191 (53.1)	

Dependent: over_surv_st	t	DECEASED	LIVING	p
	С	49 (27.7)	78 (21.7)	
	OTHERS	5 (2.8)	23(6.4)	
person_neoplasm_stt	Tumor.Free	57 (32.2)	304 (84.4)	< 0.001
	With.Tumor	105 (59.3)	36 (10.0)	
	(Missing)	15 (8.5)	20 (5.6)	
wbc	Elevated	46 (26.0)	118 (32.8)	0.011
	Low	6(3.4)	3(0.8)	
	Normal	104 (58.8)	164 (45.6)	
	(Missing)	21 (11.9)	75 (20.8)	

```
\# Droping levels with narrow distributions -> check warnings ()
# Group some levels or drop one (NULL = 'level') when grouping is not possible
kirc_clin2 <- kirc_clin %>%
     mutate(neoplasm_stg = fct_collapse(neoplasm_stg, 'Stage I-II' = c('Stage I', 'Stage II'), 'Stage II
            tumor stg = fct collapse(tumor stg, 'T1-T2' = c('T1', 'T2'), 'T3-T4' = c('T3', 'T4')),
            histology_grd = fct_collapse(histology_grd, 'G1-G2' = c('G1','G2'), 'G3-G4' = c('G3','G4'))
            hemoglobin = fct_collapse(hemoglobin, 'Not.Low' = c('Normal', 'Elevated')),
            serum_ca = fct_collapse(serum_ca, 'Not.Low' = c('Normal', 'Elevated')),
            wbc = fct_collapse(wbc, 'Not.Elevated' = c('Low', 'Normal')))
kirc_clin2 <- kirc_clin2 %>%
     mutate(histology_grd = fct_recode(histology_grd, NULL = 'GX'),
            tumor_lateral = fct_recode(tumor_lateral, NULL = 'Bilateral'),
            race = fct_recode(race, NULL = 'Asian'))
table_char2 <- kirc_clin2 %>%
  summary_factorlist(dependent, explanatory_char, p=TRUE,
                     add_dependent_label=TRUE, na_include = TRUE)
knitr::kable(table_char2, row.names=FALSE, align=c("1", "1", "r", "r", "r"))
```

Dependent: over_surv_stt		DECEASED	LIVING	p
metastasis_stg	M0	110 (62.1)	316 (87.8)	< 0.001
_	M1	64 (36.2)	15(4.2)	
	MX	3(1.7)	27(7.5)	
	(Missing)	0(0.0)	2(0.6)	
lymph_stg	N0	85 (48.0)	155 (43.1)	0.001
	N1	12 (6.8)	5(1.4)	
	NX	80 (45.2)	200 (55.6)	
neoplasm_stg	Stage I-II	58 (32.8)	268 (74.4)	< 0.001
	Stage III-IV	118 (66.7)	90 (25.0)	
	(Missing)	1(0.6)	2(0.6)	
tumor_stg	T1-T2	71 (40.1)	273 (75.8)	< 0.001
-	T3-T4	106 (59.9)	87 (24.2)	
disease_free_stt	DiseaseFree	0(0.0)	311 (86.4)	< 0.001
	Recurred/Progressed	78 (44.1)	49 (13.6)	
	(Missing)	99 (55.9)	0(0.0)	
ethnicity	hispanic/latino	3(1.7)	23(6.4)	0.017
	not hispanic/latino	132 (74.6)	227(63.1)	

Dependent: over_surv_stt		DECEASED	LIVING	p
	(M::)			P
1-1-4-1	(Missing)	42 (23.7)	110 (30.6)	<0.001
histology_grd	G1-G2	45 (25.4)	199 (55.3)	< 0.001
	G3-G4	131 (74.0)	154 (42.8)	
1 11:	(Missing)	1(0.6)	7(1.9)	₂ 0,001
hemoglobin	Not.Low	46 (26.0)	145 (40.3)	< 0.001
	Low	118 (66.7)	145 (40.3)	
1	(Missing)	13 (7.3)	70 (19.4)	0.000
neoadj_therapy	No	167 (94.4)	352 (97.8)	0.069
	Yes	10 (5.6)	8 (2.2)	
prior_cancer	No	153 (86.4)	306 (85.0)	0.753
	Yes	$24\ (13.6)$	54 (15.0)	
tumor_lateral	Left	98 (55.4)	155 (43.1)	0.010
	Right	79(44.6)	204 (56.7)	
	(Missing)	0 (0.0)	1(0.3)	
platelet	Elevated	$30 \ (16.9)$	8(2.2)	< 0.001
	Low	20 (11.3)	26 (7.2)	
	Normal	108 (61.0)	252 (70.0)	
	(Missing)	19 (10.7)	74(20.6)	
race	Black/African.american	11 (6.2)	45 (12.5)	0.032
	White	163 (92.1)	303 (84.2)	
	(Missing)	3(1.7)	12(3.3)	
serum ca	Not.Low	71 (40.1)	$90\ (25.0)$	0.028
_	Low	66 (37.3)	138 (38.3)	
	(Missing)	40 (22.6)	132 (36.7)	
gender	Female	65 (36.7)	126 (35.0)	0.767
	Male	112 (63.3)	234 (65.0)	
tissue_site	A	11 (6.2)	68 (18.9)	< 0.001
	В	112 (63.3)	191 (53.1)	,,,,,,
	C	49 (27.7)	78 (21.7)	
	OTHERS	5 (2.8)	23 (6.4)	
person_neoplasm_stt	Tumor.Free	57 (32.2)	304 (84.4)	< 0.001
person_neeplasm_see	With.Tumor	105 (59.3)	36 (10.0)	(0.001
	(Missing)	15 (8.5)	20 (5.6)	
wbc	Elevated	46 (26.0)	118 (32.8)	0.018
WBC	Not.Elevated	110 (62.1)	167 (46.4)	0.010
	(Missing)	21 (11.9)	75 (20.8)	
	(missing)	21 (11.9)	10 (20.8)	

${\bf 6.}\ {\bf saving}\ {\bf dataset}\ {\bf for}\ {\bf regression}\ {\bf model}$

```
kirc_glm <- kirc_clin2
write_csv(kirc_glm, path = "data/kirc_glm.csv")</pre>
```

Further analysis

 $\bullet\,$ A logistic regression analysis of each clinical variable weight.

sessionInfo()

```
## R version 4.0.3 (2020-10-10)
## Platform: x86_64-pc-linux-gnu (64-bit)
```

```
## Running under: Ubuntu 18.04.5 LTS
##
## Matrix products: default
## BLAS: /usr/lib/x86_64-linux-gnu/openblas/libblas.so.3
## LAPACK: /usr/lib/x86_64-linux-gnu/libopenblasp-r0.2.20.so
##
## locale:
## [1] LC_CTYPE=pt_BR.UTF-8
                                   LC NUMERIC=C
   [3] LC_TIME=pt_BR.UTF-8
                                   LC COLLATE=en US.UTF-8
                                   LC_MESSAGES=en_US.UTF-8
  [5] LC_MONETARY=pt_BR.UTF-8
## [7] LC_PAPER=pt_BR.UTF-8
                                   LC_NAME=C
                                   LC_TELEPHONE=C
## [9] LC_ADDRESS=C
## [11] LC_MEASUREMENT=pt_BR.UTF-8 LC_IDENTIFICATION=C
##
## attached base packages:
## [1] stats
                 graphics grDevices utils
                                               datasets methods
                                                                    base
##
## other attached packages:
## [1] plotly_4.9.2.1 GGally_2.0.0
                                                         rstatix 0.6.0
                                        ggpubr_0.4.0
## [5] finalfit 1.0.2
                        skimr 2.1.2
                                        forcats 0.5.0
                                                         stringr 1.4.0
## [9] dplyr_1.0.2
                        purrr_0.3.4
                                        readr_1.4.0
                                                         tidyr_1.1.2
## [13] tibble_3.0.3
                        ggplot2_3.3.2
                                        tidyverse_1.3.0
##
## loaded via a namespace (and not attached):
## [1] nlme 3.1-149
                                                                  RColorBrewer 1.1-2
                           fs 1.5.0
                                              lubridate_1.7.9
## [5] httr 1.4.2
                           ggsci_2.9
                                              repr_1.1.0
                                                                  tools 4.0.3
## [9] backports_1.1.10
                           utf8_1.1.4
                                              R6_2.4.1
                                                                  mgcv_1.8-33
## [13] DBI_1.1.0
                                              colorspace_1.4-1
                                                                  withr_2.3.0
                           lazyeval_0.2.2
                                                                  cli_2.0.2
## [17] tidyselect_1.1.0
                           curl_4.3
                                              compiler_4.0.3
## [21] rvest_0.3.6
                           mice_3.11.0
                                              xm12_1.3.2
                                                                  labeling_0.3
## [25] scales_1.1.1
                           digest_0.6.25
                                              foreign_0.8-79
                                                                  rmarkdown_2.4
## [29] rio_0.5.16
                           base64enc_0.1-3
                                              pkgconfig_2.0.3
                                                                  htmltools_0.5.0
## [33] highr_0.8
                           dbplyr_1.4.4
                                              htmlwidgets_1.5.2
                                                                  rlang_0.4.7
## [37] readxl_1.3.1
                                              farver_2.0.3
                                                                  generics_0.0.2
                           rstudioapi_0.11
## [41] isonlite 1.7.1
                           zip 2.1.1
                                              car 3.0-10
                                                                  magrittr 1.5
## [45] Matrix_1.2-18
                           Rcpp_1.0.5
                                              munsell_0.5.0
                                                                  fansi_0.4.1
## [49] abind 1.4-5
                           lifecycle 0.2.0
                                              stringi 1.5.3
                                                                  yaml 2.2.1
## [53] carData_3.0-4
                           plyr_1.8.6
                                              grid_4.0.3
                                                                  blob_1.2.1
## [57] crayon 1.3.4
                           lattice_0.20-41
                                              haven_2.3.1
                                                                  splines 4.0.3
## [61] hms_0.5.3
                           knitr_1.30
                                              pillar_1.4.6
                                                                  boot_1.3-25
## [65] ggsignif 0.6.0
                           reprex 0.3.0
                                              glue 1.4.2
                                                                  evaluate 0.14
## [69] data.table 1.13.0
                           modelr 0.1.8
                                              vctrs_0.3.4
                                                                  cellranger 1.1.0
                           reshape_0.8.8
                                                                  xfun 0.18
## [73] gtable 0.3.0
                                              assertthat_0.2.1
                           broom_0.7.1
                                                                  viridisLite_0.3.0
## [77] openxlsx_4.2.2
                                              survival_3.2-7
## [81] ellipsis_0.3.1
```