# Survival Analysis

## Contents

# 1 Introduction

## 1.1 Definitions

The **Survival analysis** also known as time to event analysis is used to predict the time until an event occurs.

Most important concepts for this analysis:

- **Exposure** (clock starts), time zero of the analysis for this subject.
- **Event** (clock stops),
- **Survival time**, (difference between time of Event and time of Exposure).

A Survival time can be estimated in this examples:

- Exposure (Cancer diagnostic), Event (Death )
- Exposure (Marriage), Event (Divorce)

## 1.2 Equation

Y = time-to-event

Where the Y = outcome, depends on *Time* and on the *Event* (0 = NO, 1 = YES) :

- 0 : the event didn't occured
- 1 : the event occured

# 2 Survival function, Hazard & Hazard ratio

## 2.1 The Survival function/Model

survival function $S(t) = P(T > t)$ = Probability of Survival **beyond time t**.

## 2.2 Hazard

$Hazard(Haz) = P(T < t + d \mid T > t)$ = probability of dying in the next few seconds **given alive now**.

For the Exponential survival model, the hazard function correspond to the rate of the exponential curve.

## 2.3 Hazard Ratio

$Hazard\,(HR) = \frac{Haz,x=1}{Haz,x=0}$ = relative ratio,

At a given instant in time someone who is exposed is "relative ration" times more important to someone who is not.

## 2.4 Different models

Two type of functions/models to illustrate the decrease in survival probability.

S(t) is the survival function

- **Kaplan-Meier survival model** (non-parametric)
  - Pros : Simple to interpret, can estimate S(t)
  - Cons : No functional form (no mathematical function, because of steps), can not estimate hazard ratio
- **Exponential survival model** (parametric)
  - Pros : Can estimate the S(t), and Hazard ratio
  - Cons : Not always realistic, because assumes constant hazard ( death is not constant )
- **Cox proportional Hazard model** (semi-parametric), sort of a combination of KM model and Exponential model
  - Pros : Haz can fluctuate with time, Can estimate Hazard ratio
  - Cons : Can not estimate S(t)

## 2.5 Kaplan-Meier survival model

Also known as Product-Limit Method, or the life table method.

This is a non-parametric curve, explains the selected data. The ticks are censored data

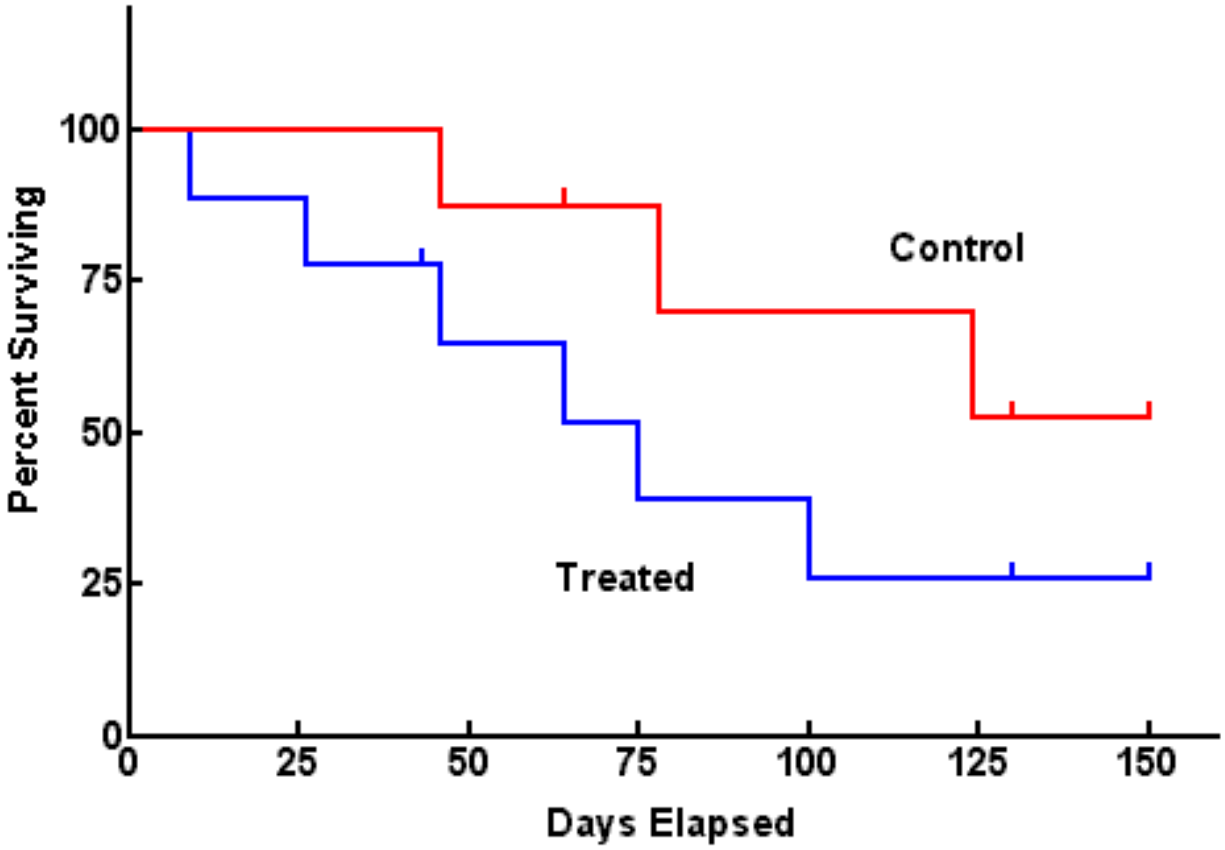



Figure 1: Kaplan Meier Curve

## 2.6 More examples of use

In Health, Time to:

- Death
- Device failure
- Re-admission

In industry, Time to:

- Component failure
- Business failure
- staff promotion

In marriage, Time to:

- Divorce
- Second child

# 3 Censoring and truncation

## 3.1 Definitions

**Censoring** : Censoring occurs when we don't know the exact time-to-event for an included observation. Lack of some part of the information.

There are 3 different types of censoring :

- Right censoring (time to event greater than a value), this type of censoring could sometimes be informative when the censoring is actually correlated to the expected event (consequence).
- Left censoring (time to event less than a value)
- Interval censoring ( time to event between two values)

An example of right censoring is a time-to-event that continues after the experiment ( patient that is still alive a the end of the study).

**Truncation** : Truncation occurs when observation are excluded by virtue of their time-to-event. Short or Long time events that where not measured.

There are 2 different types of truncation :

- left truncation ( short time-to-event values, small values that where not measured )
- right truncation ( long time-to-event values, large values that where not measured )

The whole data set can be truncated, whereas data points can be censored.

# 4 Kaplan Meier Model in R

```
rm(list = ls())

library(tidyverse)
library(survival)

time   <- c(2,4,6,8,11,15,16,18,18,20,22,22,25,27,28,32,32,34,34)
death  <- c(1,1,0,1,1,1,1,0,0,1,0,1,1,1,1,0,1,0,0) # Censoring or not, 1 = died, 0 = censored
over40 <- c(1,1,0,1,1,1,1,0,0,1,0,1,0,1,1,0,1,1,0)   # Is over 40 or not, 1 = YES, 0 = NO

df <- tibble(time,death,over40)
```

## 4.1 Kaplan Meier Model with no X variable

## 4.2 Summary

```
# We use ~1 when there is no X variable ( additional categorical variable )
km.model <- survfit(Surv(time = time, event = death) ~ 1,
                    type = "kaplan-meier")  # Kaplan-Meier is the default value

km.model
```

```
## Call: survfit(formula = Surv(time = time, event = death) ~ 1, type = "kaplan-meier")
##
##       n events median 0.95LCL 0.95UCL
## [1,] 19     12     25      16      NA
```

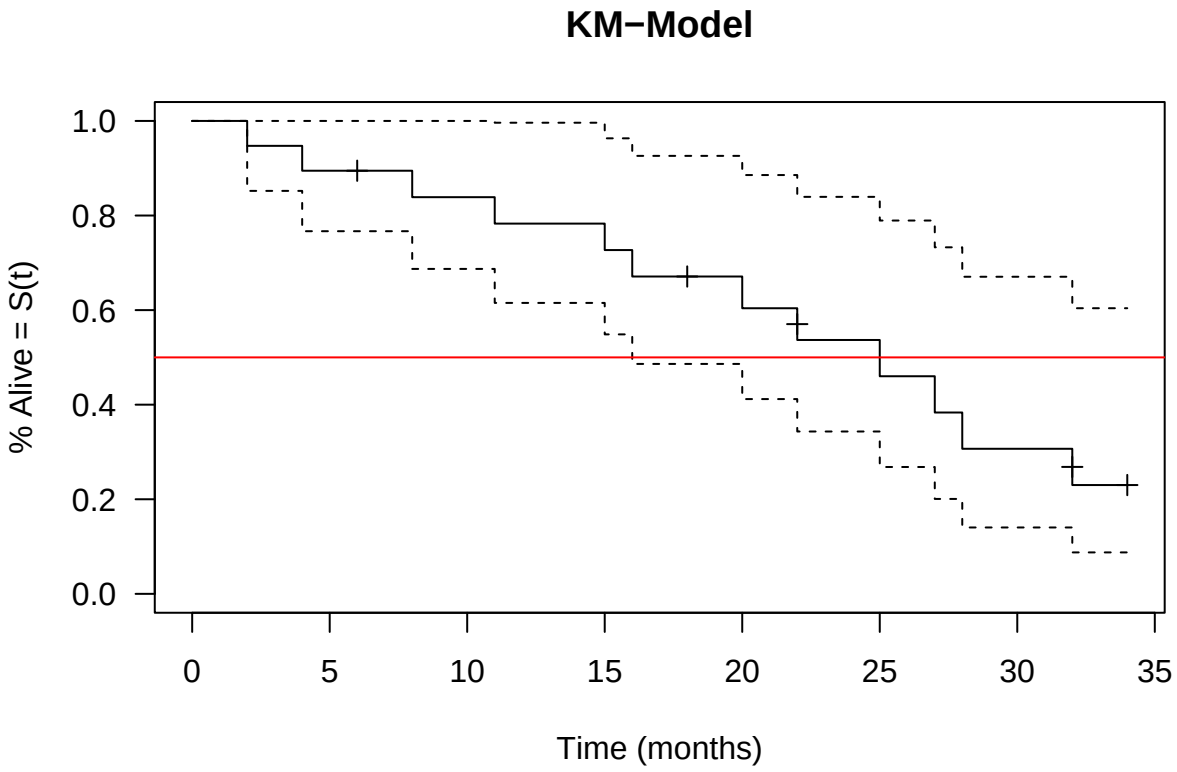
To visualize the survival at specific time, and confidence intervals.

```
summary(km.model)
```

```
## Call: survfit(formula = Surv(time = time, event = death) ~ 1, type = "kaplan-meier")
##
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##     2     19       1    0.947  0.0512       0.8521        1.000
##     4     18       1    0.895  0.0704       0.7669        1.000
##     8     16       1    0.839  0.0854       0.6871        1.000
##    11     15       1    0.783  0.0963       0.6152        0.996
##    15     14       1    0.727  0.1044       0.5487        0.963
##    16     13       1    0.671  0.1103       0.4862        0.926
##    20     10       1    0.604  0.1179       0.4119        0.886
##    22      9       1    0.537  0.1224       0.3433        0.839
##    25      7       1    0.460  0.1267       0.2682        0.789
##    27      6       1    0.383  0.1267       0.2007        0.733
##    28      5       1    0.307  0.1224       0.1404        0.671
##    32      4       1    0.230  0.1133       0.0876        0.604
```

### 4.3 Kaplan-Meier curve

```
plot(
  km.model,     # used model
  conf.int = T,    # include confidence intervals
  xlab = "Time (months)",
  ylab = "% Alive = S(t)",
  main = "KM-Model",
  las = 1,        # rotatates the values on the y axis for better readability
  mark.time = T  # adds the censored values to the graph as a tick
  )

abline(h = 0.5, col = "red")
```



## 4.4 Kaplan-Meier model with an X variable

## 4.5 Summary

```
# We use ~1 when there is no X variable ( additional categorical variable )
km.model2 <- survfit(Surv(time = time, event = death) ~ over40,
                     type = "kaplan-meier")  # Kaplan-Meier is the default value

km.model2
```

```
## Call: survfit(formula = Surv(time = time, event = death) ~ over40,
##     type = "kaplan-meier")
##
##           n events median 0.95LCL 0.95UCL
## over40=0  7      1     NA      25      NA
## over40=1 12     11     18      11      NA
```

To visualize the survival at specific time, and confidence intervals.

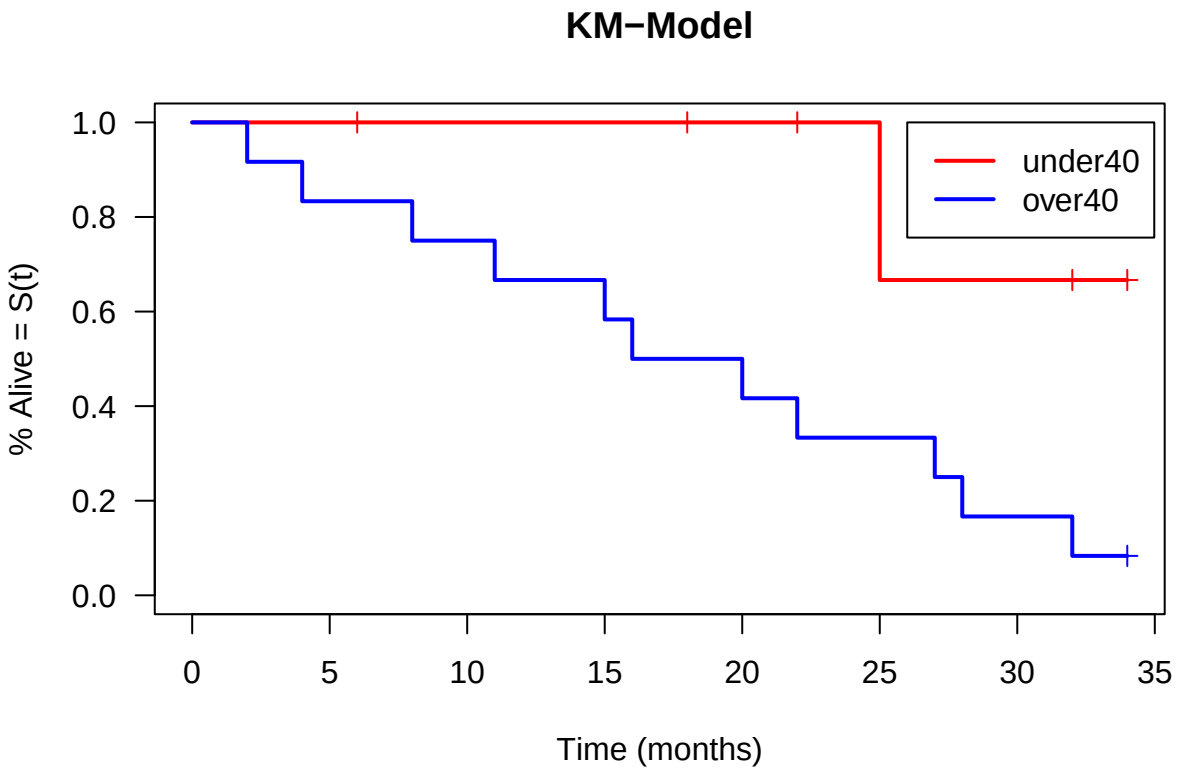
```
summary(km.model2)
```

```
## Call: survfit(formula = Surv(time = time, event = death) ~ over40,
##     type = "kaplan-meier")
##
##                 over40=0
##         time       n.risk      n.event     survival      std.err lower 95% CI
##       25.000        3.000        1.000        0.667        0.272        0.300
## upper 95% CI
##        1.000
##
##                 over40=1
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##     2     12       1   0.9167  0.0798       0.7729        1.000
##     4     11       1   0.8333  0.1076       0.6470        1.000
##     8     10       1   0.7500  0.1250       0.5410        1.000
##    11      9       1   0.6667  0.1361       0.4468        0.995
##    15      8       1   0.5833  0.1423       0.3616        0.941
##    16      7       1   0.5000  0.1443       0.2840        0.880
##    20      6       1   0.4167  0.1423       0.2133        0.814
##    22      5       1   0.3333  0.1361       0.1498        0.742
##    27      4       1   0.2500  0.1250       0.0938        0.666
##    28      3       1   0.1667  0.1076       0.0470        0.591
##    32      2       1   0.0833  0.0798       0.0128        0.544
```

## 4.6 Kaplan-Meier curve with an X variable

```
plot(
  km.model2,    # used model
  conf.int = F,   # include confidence intervals
```

```
  xlab = "Time (months)",
  ylab = "% Alive = S(t)",
  main = "KM-Model",
  col = c("red","blue"),    # add colors to the plots
  lwd = 2,        # makes the line a bit more thick
  las = 1,        # rotatates the values on the y axis for better readability
  mark.time = T  # adds the censored values to the graph as a tick
  )

legend(26,     # x coordinate for the box
       1,      # y coordinate for the box
       legend = c("under40","over40"),  # Names for the legend
       lty = 1, # linetype
       lwd = 2, # linewidth
       col = c("red","blue"),
       bty = "",  # boxtype shape
       cex = 1    # boxfont size
       )
```




## 4.7 The LOG-RANK-TEST

The logrank test assesses whether the KM survival curves from two subpopulation are significantly different. Comparing the survival curves to see if they are different.

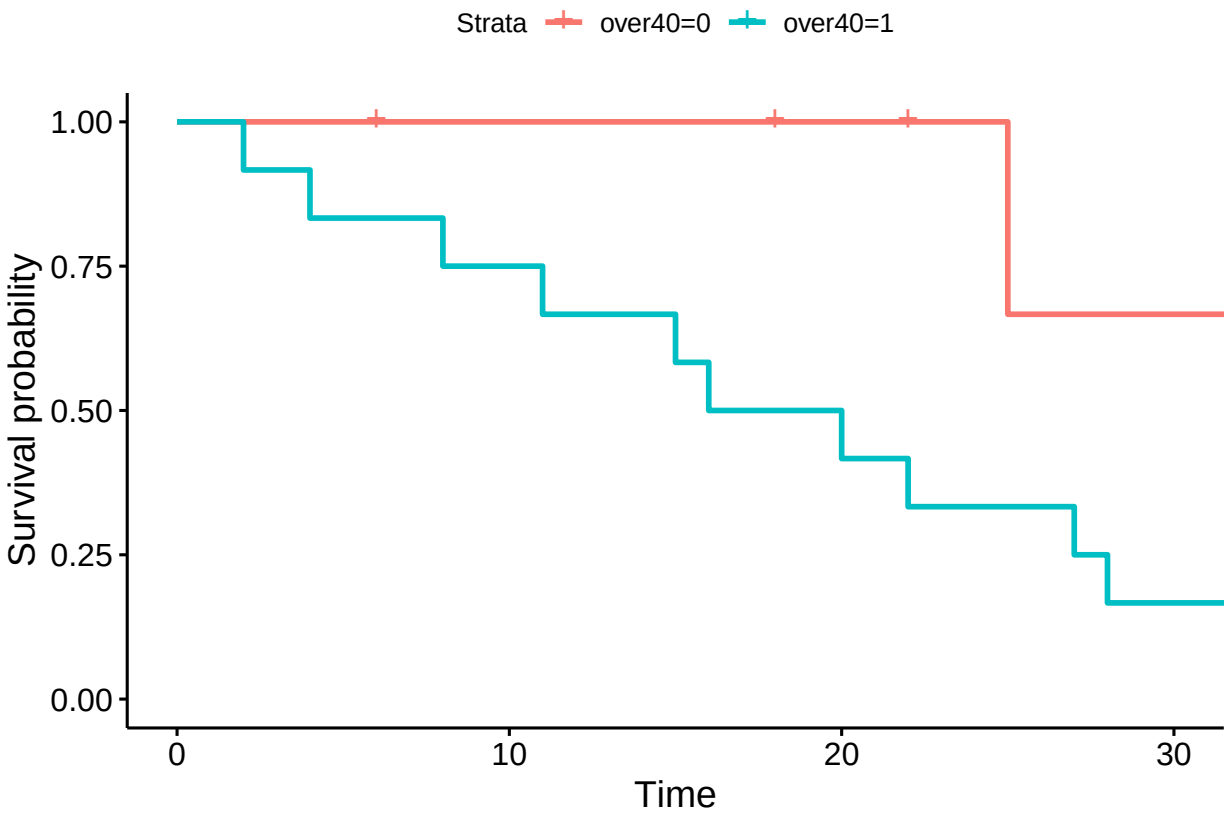
$H_0$: surivival in two groups is **the same**. $H_1$: survival in the two groups is **not the same**.

```
survdiff(Surv(time,death)~ over40) # This can work with also more than 2 levels ( )
```

```
## Call:
## survdiff(formula = Surv(time, death) ~ over40)
##
##            N Observed Expected (O-E)^2/E (O-E)^2/V
## over40=0  7        1     4.93      3.13      5.36
## over40=1 12       11     7.07      2.18      5.36
##
##  Chisq= 5.4  on 1 degrees of freedom, p= 0.02
```

### 4.8 Exemple of plot with ggplot2

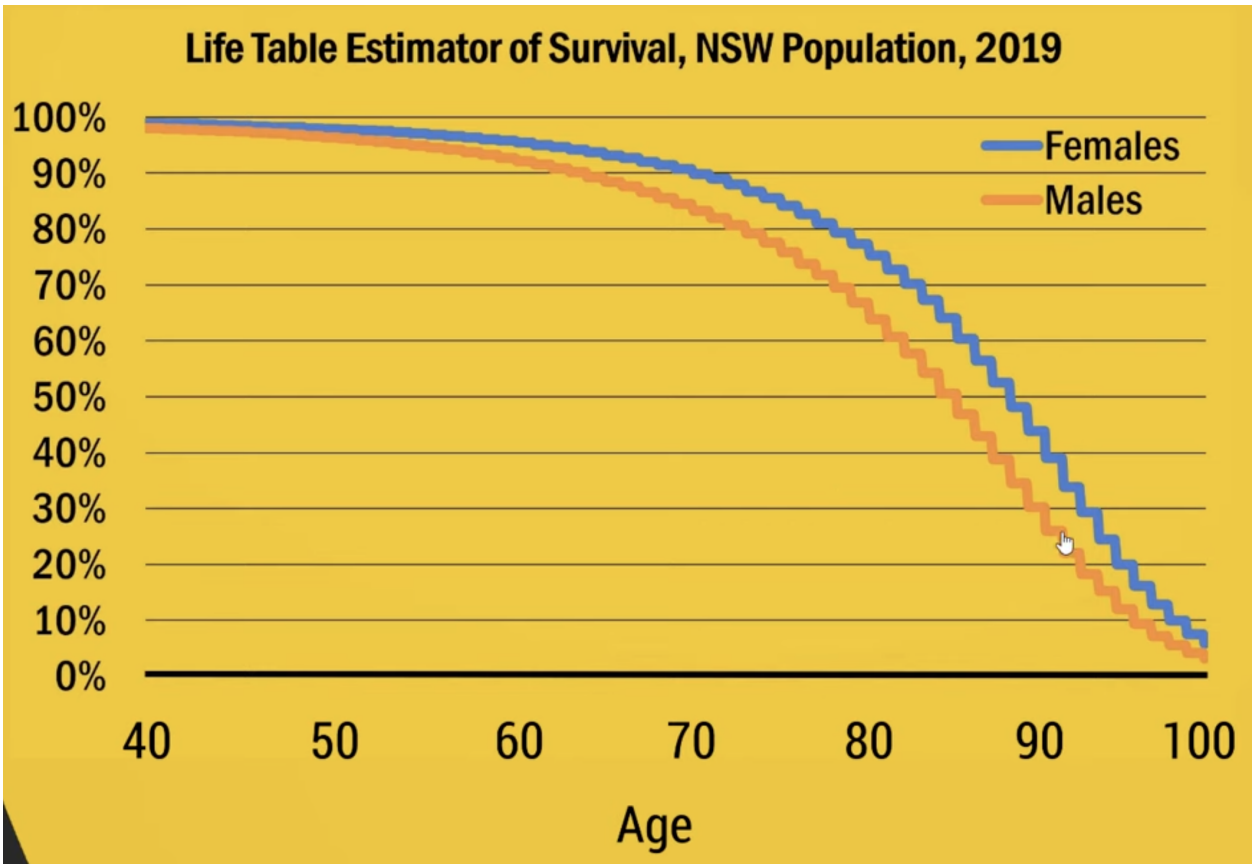
```
km.model2 <- survfit(Surv(time = time, event = death) ~ over40,
                     type = "kaplan-meier")  # Kaplan-Meier is the default value

p <- survminer::ggsurvplot(fit = km.model2,data = df)

p
```



# 5 Life tables

## 5.1 Definitions

Life tables illustrate the pattern of survivorship of a population by considering the probability of death at each consecutive age.




Input :

- population by age group
- deaths in each age group

Output :

- the survival functions at each age
- conditional life expectancy at each age ( probability of being alive)
- median, mean quantile survival

# 6 Kaplan-Meier Curves and Log-rank Test

## 6.1 Calculating the steps

It's a **non-parametric** estimator of survival. Doesn't have an estimator ( like the mean or the standard deviation for an normal distribution ). A Kaplan-Meier curve looks more like steps than a curve, and doesn't use parameters, it represents the data.

| Wombat | Survival Time | Died? (1=died) |
|---|---|---|
| F | 4 | 1 |
| G | 6 | 1 |
| J | 8 | 0 |
| H | 11 | 1 |
| A | 15 | 1 |
| E | 15 | 1 |
| C | 20 | 1 |
| I | 20 | 0 |
| D | 25 | 1 |
| B | 31 | 0 |

| Time | n | d | Calculation | Survival, S(t) |
|---|---|---|---|---|
| $0 \le t < 4$ | 10 | 0 | **1** | **1** |
| $4 \le t < 6$ | 10 | 1 | **9/10** x 1 | 0.9 |
| $6 \le t < 8$ | 9 | 1 | **8/9** x 0.9 | 0.8 |
| $8 \le t < 11$ | 8 | 0 | **8/8** x 0.8 | 0.8 |
| $11 \le t < 15$ | 7 | 1 | **6/7** x 0.8 | 0.686 |
| $15 \le t < 20$ | 6 | 2 | **4/6** x 0.686 | 0.457 |
| $20 \le t < 25$ | 4 | 1 | **3/4** x 0.457 | 0.342 |
| $25 \le t < 31$ | 2 | 1 | **1/2** x 0.342 | 0.171 |

Figure 2: Survival Table

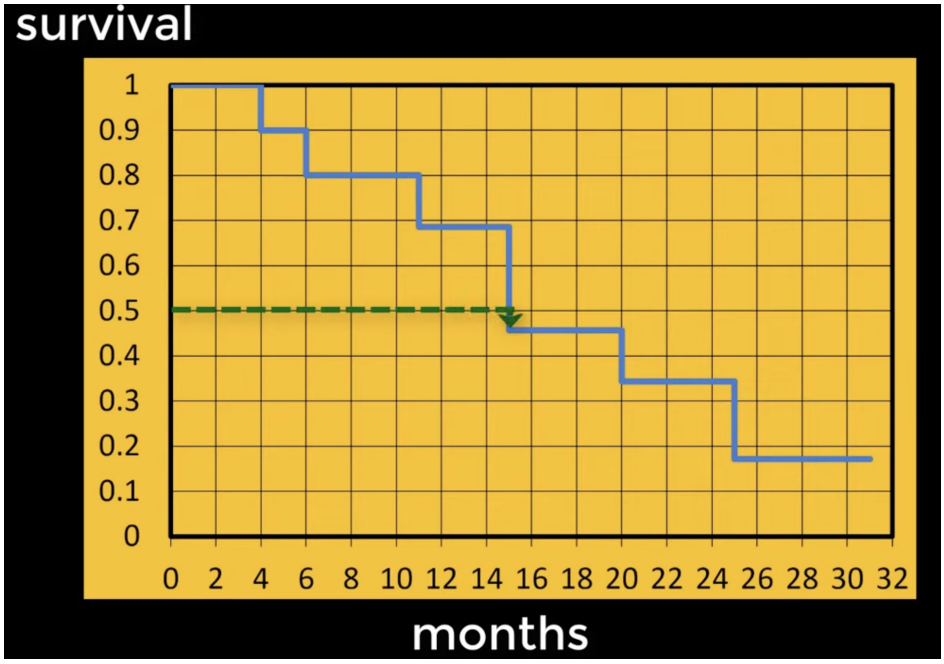



Figure 3: Survival Curve