gClinBiomarker: Example Use Cases

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Loading packages and data

```
if (!require(gClinBiomarker)) {
   install_github("RPackages/gClinBiomarker", host="https://github.roche.com/api/v3")
   library(gClinBiomarker)
}

library(knitr)
library(devtools)
library(ggplot2)
data(input)
sample.data <- input</pre>
```

Example data set

```
head(sample.data)
```

```
Patient.ID Sample.ID Arm Age Weight ECOG Sex Baseline.SLD
##
                                                                       Country
## 1
         PID001
                   SID001 TRT
                                    61.0
                              40
                                                F
                                                      550.4970 Western Europe
## 2
        PID002
                   SID002 TRT
                                    87.0
                                                      549.7751
## 3
        PID003
                  SID003 TRT
                                    57.6
                                            1 M
                                                      548.8829 Western Europe
                               53
## 4
         PID004
                   SID004 TRT
                               44
                                    57.0
                                                F
                                                      549.6050
                                                F
## 5
         PID005
                                            2
                   SID005 TRT
                               49
                                    72.5
                                                      551.5498
                                                                         Other
         PID006
                   SID006 TRT
                               62
                                    76.0
                                            0
                                                      549.2565
##
    CD8.ihc KRAS.mutant KRAS.exprs
                                          OS
                                                  PFS Response BEP OS.event
## 1
          3
                  Mutant
                             171.25 9.691992 5.782341
                                                             PR
                                                                 1
          2
                                                             PD
## 2
              Wild Type
                               2.77 4.435318 1.412731
                                                                 1
                                                                            1
## 3
          3
              Wild Type
                              61.82 9.691992 1.215606
                                                             PD
                                                                 1
                                                                           0
## 4
                                                             PD
                                                                           0
          1
                  Mutant
                              71.51 1.905544 1.905544
                                                                  1
## 5
          NA
                    <NA>
                                 NA 2.628337 2.628337
                                                             SD
                                                                  0
                                                                            1
## 6
           2
                  Mutant
                              44.63 4.829569 4.139630 NON CR/PD
##
    PFS.event Lab_ontrt
## 1
            0 28.993922
## 2
            1 9.890427
## 3
            1 26.896020
## 4
            1 5.421392
## 5
             1 14.741382
## 6
            0 16.957035
```

```
str(sample.data)
```

```
## 'data.frame': 550 obs. of 19 variables:
## $ Patient.ID : chr "PID001" "PID002" "PID003" "PID004" ...
## $ Sample.ID : chr "SID001" "SID002" "SID003" "SID004" ...
## $ Arm
            : Factor w/ 2 levels "CTRL", "TRT": 2 2 2 2 2 2 2 2 1 ...
## $ Age
                : int 40 60 53 44 49 62 70 49 62 45 ...
## $ Weight
               : num 61 87 57.6 57 72.5 76 46 69.3 65 54 ...
## $ ECOG
                : int 0 1 1 0 2 0 0 1 0 1 ...
               : chr "F" "F" "M" "F" ...
## $ Sex
## $ Baseline.SLD: num 550 550 549 550 552 ...
## $ Country : Factor w/ 3 levels "Other", "USA",..: 3 2 3 2 1 1 3 3 3 1 ...
## $ CD8.ihc
               : num 3 2 3 1 NA 2 NA 1 NA NA ...
## $ KRAS.mutant : Factor w/ 2 levels "Mutant", "Wild Type": 1 2 2 1 NA 1 NA 2 NA NA ...
## $ KRAS.exprs : num 171.25 2.77 61.82 71.51 NA ...
## $ OS
               : num 9.69 4.44 9.69 1.91 2.63 ...
## $ PFS
               : num 5.78 1.41 1.22 1.91 2.63 ...
## $ Response : Factor w/ 6 levels "CR", "NE", "NON CR/PD",...: 5 4 4 4 6 3 4 3 4 6 ...
## $ BEP
           : num 1 1 1 1 0 1 0 1 0 0 ...
## $ OS.event : int 0 1 0 0 1 0 0 0 1 0 ...
## $ PFS.event : int 0 1 1 1 1 0 1 0 1 0 ...
## $ Lab ontrt : num 28.99 9.89 26.9 5.42 14.74 ...
```

SummaryVars(): Summarize demographics variables (check demographics imbalance)

Default

	All(CTRL)	BEP(CTRL)	All(TRT)	BEP(TRT)
Age				
N	182	81	368	176
Mean	52.54	53.1	54.03	54.42
Median	51.5	52	54	54
Min-Max	2785	3285	3089	3389
NA's	0	0	0	0
Sex				
Total (non-NA)	182	81	368	176
NA's	0	0	0	0
F	89 (48.9%)	39 (48.15%)	184 (50%)	90 (51.14%)
M	93 (51.1%)	42~(51.85%)	184 (50%)	86 (48.86%)

Compare to non-BEP instead of ITT

	BEP_1(CTRL)	BEP_0(CTRL)	BEP_1(TRT)	BEP_0(TRT)
Age				
N	81	101	176	192
Mean	53.1	52.09	54.42	53.67
Median	52	50	54	54
Min-Max	3285	2782	3389	3079
NA's	0	0	0	0
Sex				
Total (non-NA)	81	101	176	192
NA's	0	0	0	0
F	39~(48.15%)	50 (49.5%)	90 (51.14%)	94~(48.96%)
M	$42 \ (51.85\%)$	51 (50.5%)	86 (48.86%)	98 (51.04%)

Allow testing

	All(CTRL)	BEP(CTRL)	pvalue(CTRL)	All(TRT)	BEP(TRT)	pvalue(TRT)
Age						
N	182	81	0.5	368	176	0.69
Mean	52.54	53.1		54.03	54.42	
Median	51.5	52		54	54	
Min-Max	2785	3285		3089	3389	
NA's	0	0		0	0	
Sex						
Total (non-NA)	182	81	0.88	368	176	0.75
NA's	0	0		0	0	
F	89 (48.9%)	39~(48.15%)		184~(50%)	90 (51.14%)	
M	93 (51.1%)	42~(51.85%)		184 (50%)	86 (48.86%)	

Reorder TRT/CTRL arm in display

	All(TRT)	BEP(TRT)	All(CTRL)	BEP(CTRL)
Age				
N	368	176	182	81
Mean	54.03	54.42	52.54	53.1
Median	54	54	51.5	52
Min-Max	3089	3389	2785	3285
NA's	0	0	0	0
Sex				
Total (non-NA)	368	176	182	81
NA's	0	0	0	0
F	184 (50%)	90 (51.14%)	89 (48.9%)	39 (48.15%)
M	184 (50%)	86 (48.86%)	93 (51.1%)	42 (51.85%)

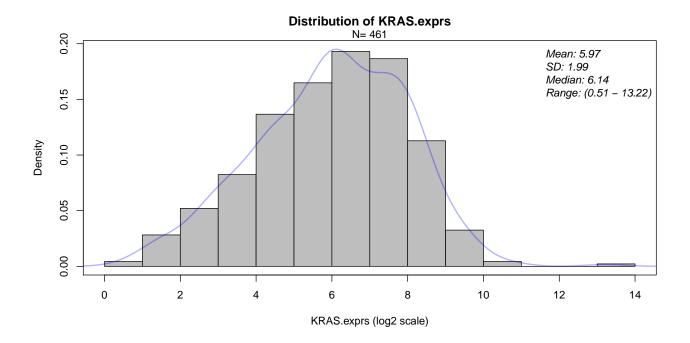
Combine trt arms

	All	BEP
Age		
N	550	257
Mean	53.53	54
Median	53	54
Min-Max	2789	3289
NA's	0	0
Sex		
Total (non-NA)	550	257
NA's	0	0
F	273 (49.64%)	129 (50.19%)
M	277 (50.36%)	128 (49.81%)

PlotProperty(): Plot biomarker, clinical covariate property and their association

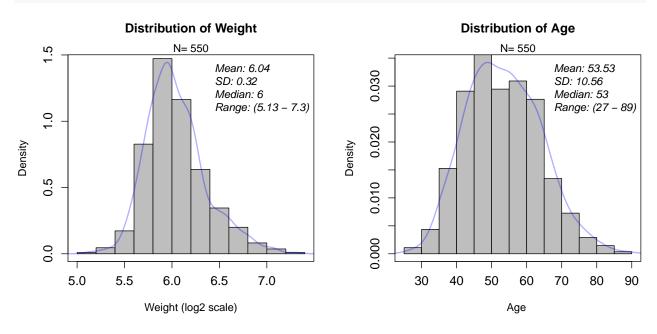
Numeric biomarker variable. No clinical variables. Log transformation.

```
PlotProperty(data=input, biomarker.var="KRAS.exprs", biomarker.class="numeric", log2=TRUE)
```



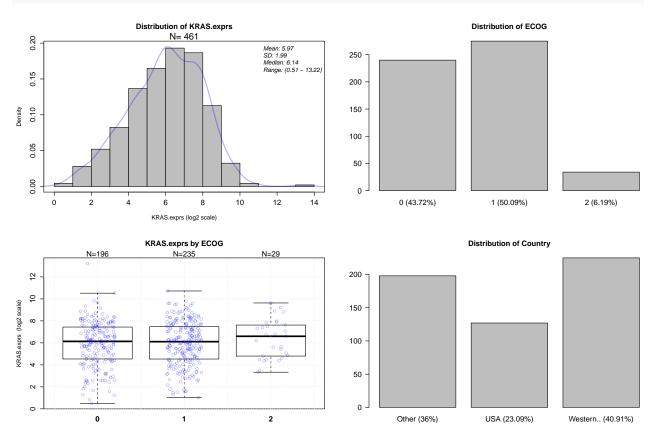
No biomarker variable. Two numeric clinical variables. Log transformation for one varible.

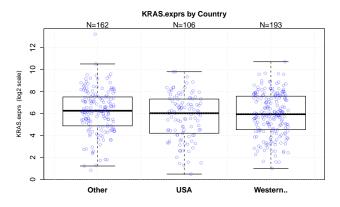
```
PlotProperty(data=input, biomarker.var=NULL, biomarker.class=NULL, var=c("Weight", "Age"), var.class=c("numeric", "numeric"), log2=c(TRUE, FALSE), par.param = list(mfrow=c(1,2), cex.axis=1.2))
```



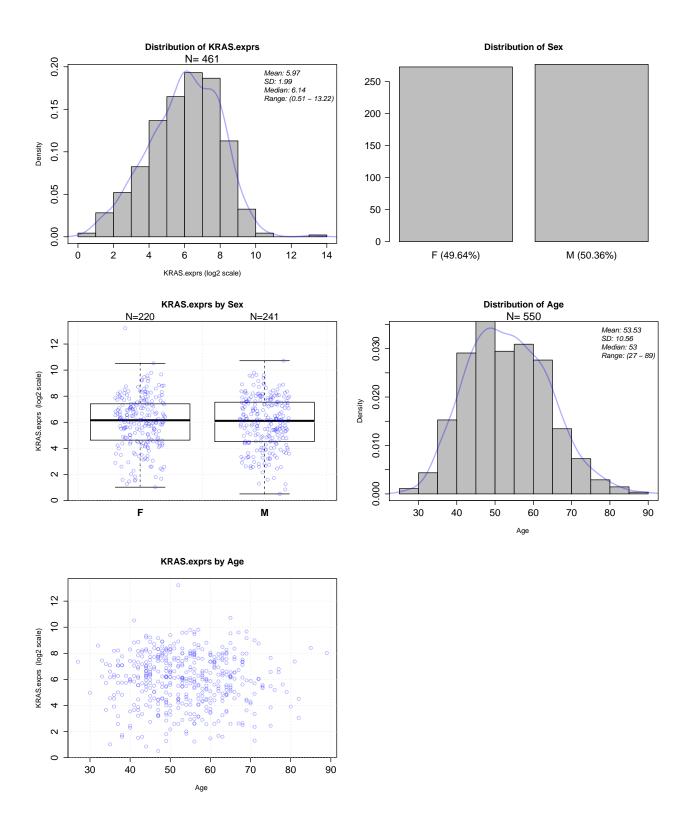
Numeric biomarker variable. Two clinical categorical variables. Log transformation for numeric variable.

```
PlotProperty(data=input, biomarker.var="KRAS.exprs", biomarker.class="numeric", var=c("ECOG", "Country"), var.class=c("categorical", "categorical"), log2=TRUE, par.param = list(mfrow=c(3,2), cex.axis=1.2), show.clinical.uni=TRUE)
```





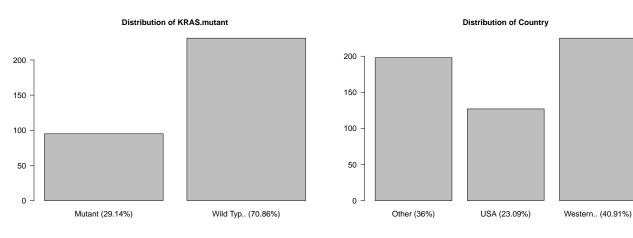
Numeric biomarker variable. Two clinical variables: one is categorocal, second is numeric. Log transformation for biomarker (numeric) variable.



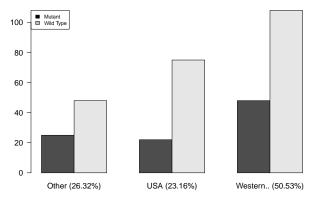
Categorical biomarker variable. Categorical clinical variable.

```
PlotProperty(data=input, biomarker.var="KRAS.mutant", biomarker.class="categorical", var="Country", var.class="categorical",
```

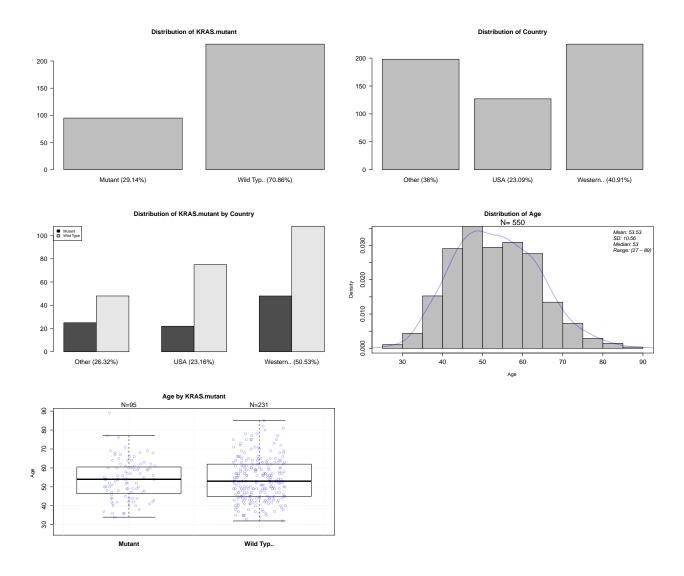




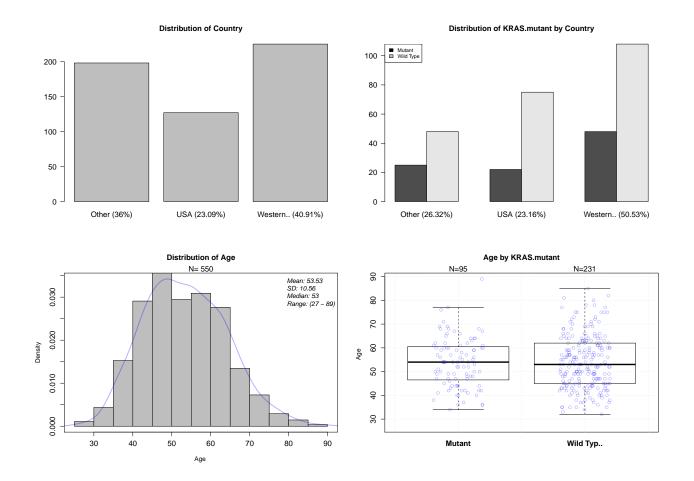
Distribution of KRAS.mutant by Country



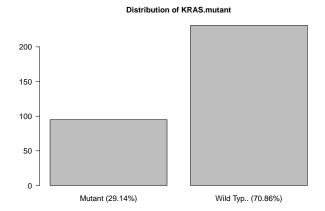
Categorial biomarker variable. Categorical and numeric clinical variables. No log transformation.

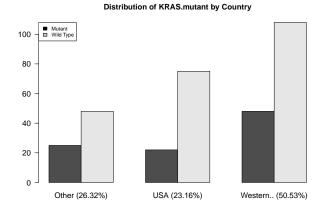


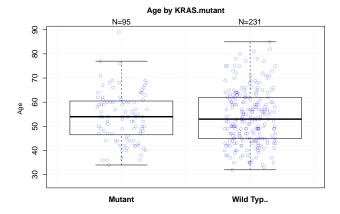
Categorial biomarker variable. Categorical and numeric clinical variables. No log transformation. Don't plot biomarker variable but plot clinical variables and association between biomarker and clinical variables.



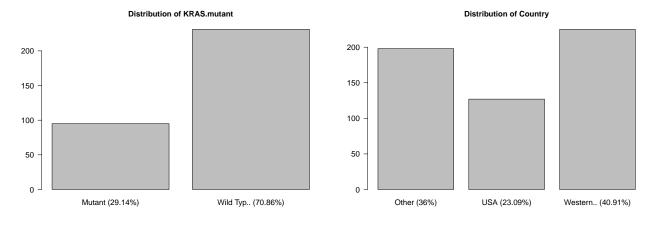
Categorial biomarker variable. Categorical and numeric clinical variables. No log transformation. Don't plot clinical variables but plot biomarker variable and association between biomarker and clinical variables.

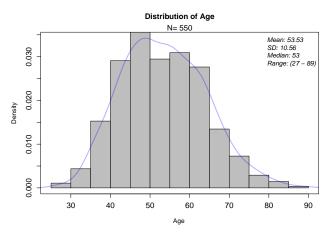




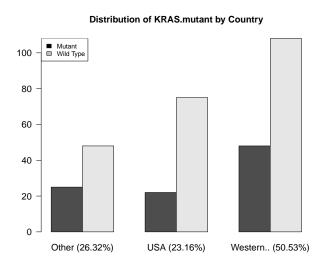


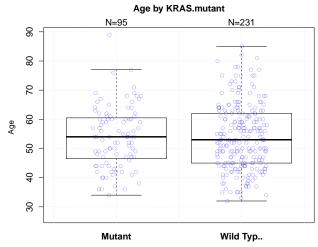
Categorial biomarker variable. Categorical and numeric clinical variables. No log transformation. Don't plot association between variables but plot biomarker and clinical variables.



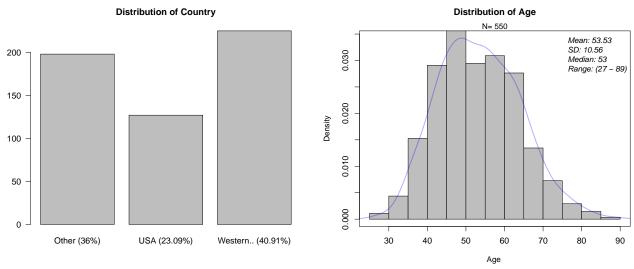


Categorial biomarker variable. Categorical and numeric clinical variables. No log transformation. Plot only association between variables.



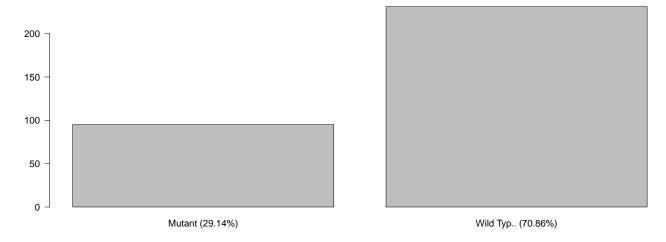


Categorial biomarker variable. Categorical and numeric clinical variables. No log transformation. Plot only clinical variables.



Categorial biomarker variable. Categorical and numeric clinical variables. No log transformation. Plot only biomarker variable.

Distribution of KRAS.mutant



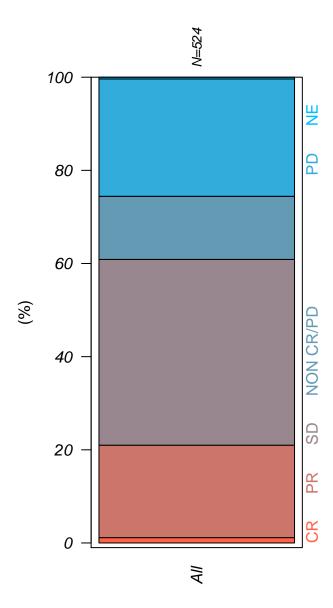
PlotRspBar(): Compare response outcome across different population

Plot response of one population

```
PlotRspBar (input, outcome.var="Response", rsp.levels=c("CR", "PR", "SD", "NON CR/PD", "PD", "NE"))
```

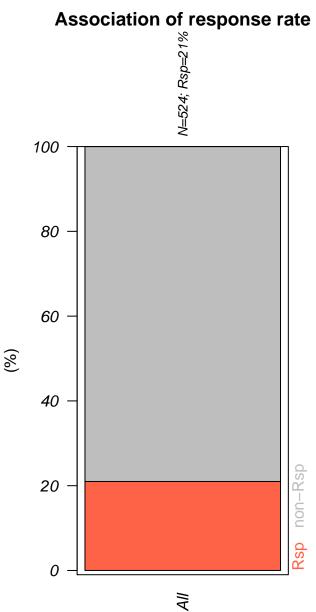
entries with missing outcome.var are removed! 524 entries left

Association of response rate



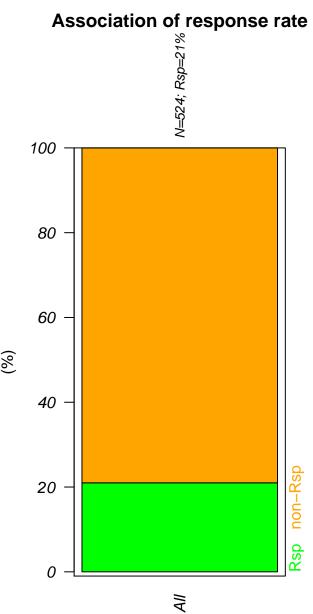
Plot response of one population, binarize outcome (classify classes to responder vs non responder)

```
PlotRspBar (input, outcome.var="Response",
            binary=TRUE,
            rsp.response = c("CR","PR"),
            rsp.nonresponse = c("SD", "PD", "NON CR/PD", "NE", NA))
```



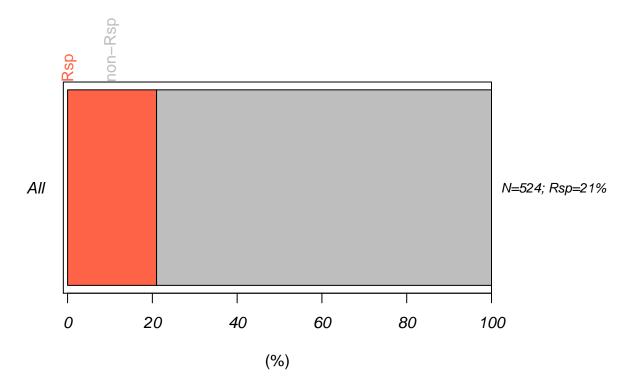
Change color

```
PlotRspBar (input, outcome.var="Response",
            binary=TRUE,
            rsp.response = c("CR", "PR"),
            rsp.nonresponse = c("SD", "PD", "NON CR/PD", "NE", NA),
            col=c("green","orange"))
```



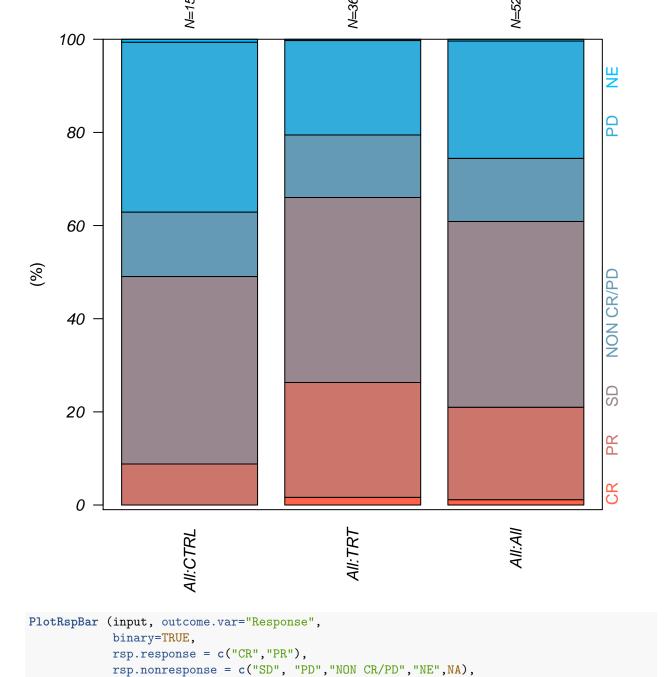
Plot horizontally

entries with missing outcome.var are removed! 524 entries left



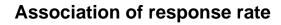
By arm

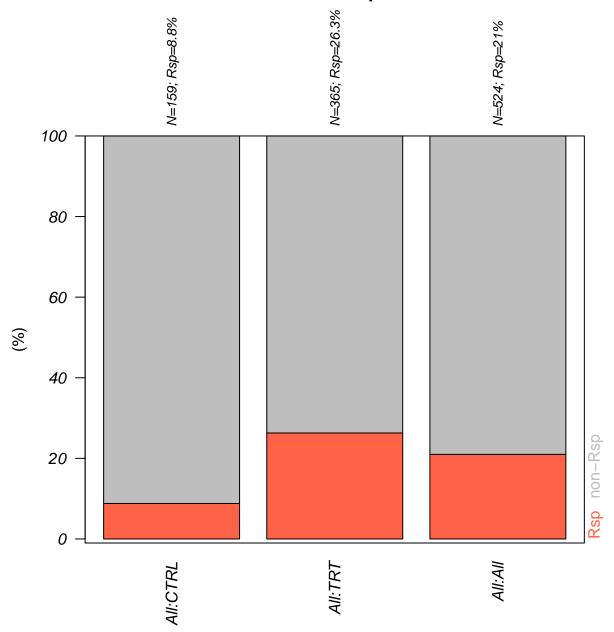
Association of response rate



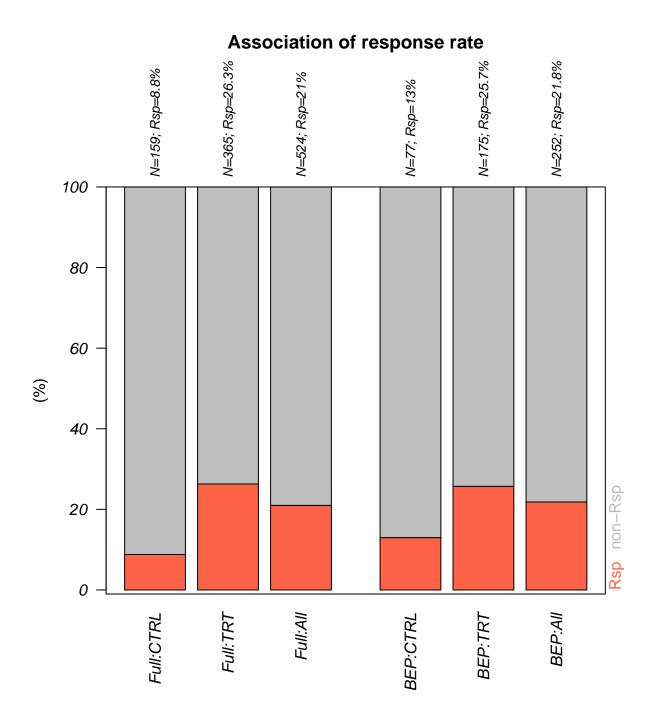
entries with missing outcome.var are removed! 524 entries left

trt="Arm")

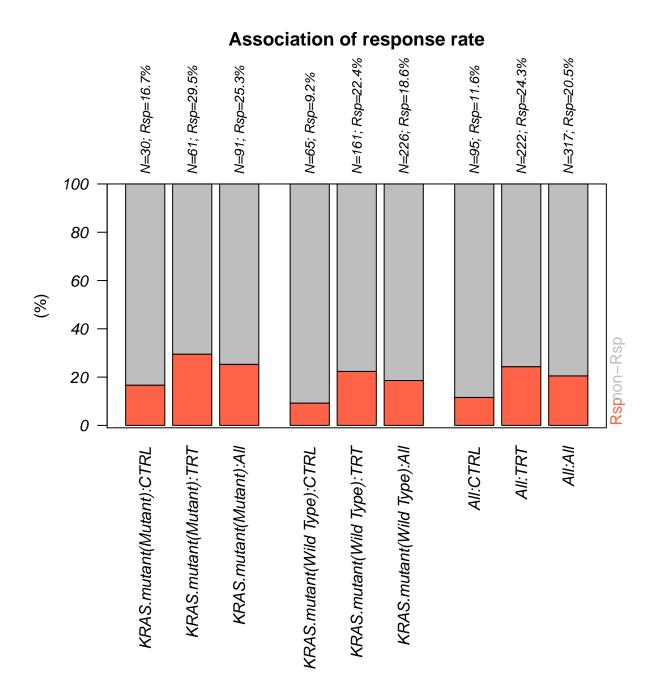




Compare full population vs BEP

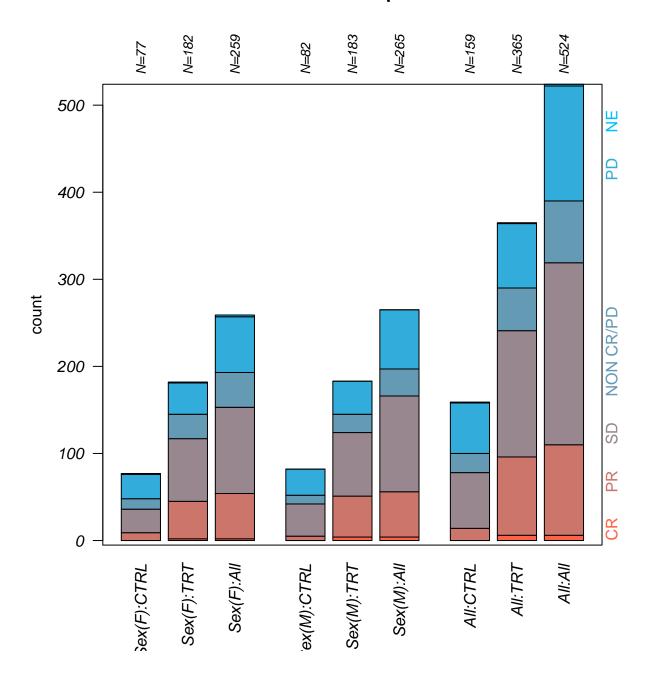


${\bf Compare~subgroups}$



Plot count instead of percentage

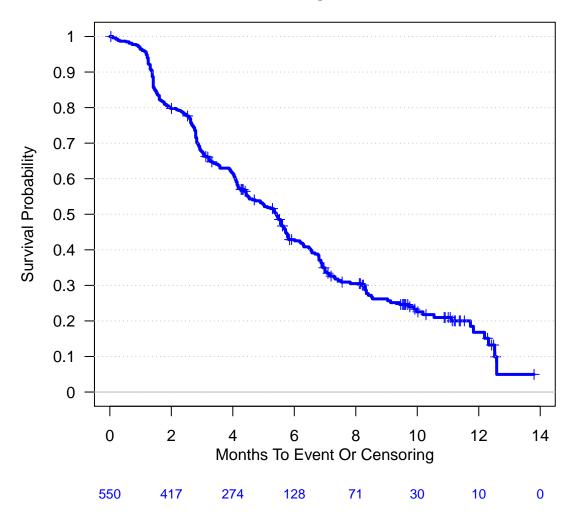
Association of response rate



PlotKM(): Plot KM curves for subpopulations

Without subgroup

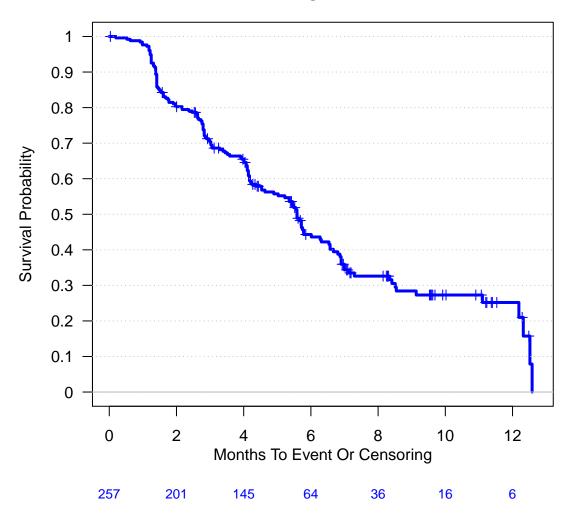
PFS ITT



[1] ""

Without subgroup, BEP

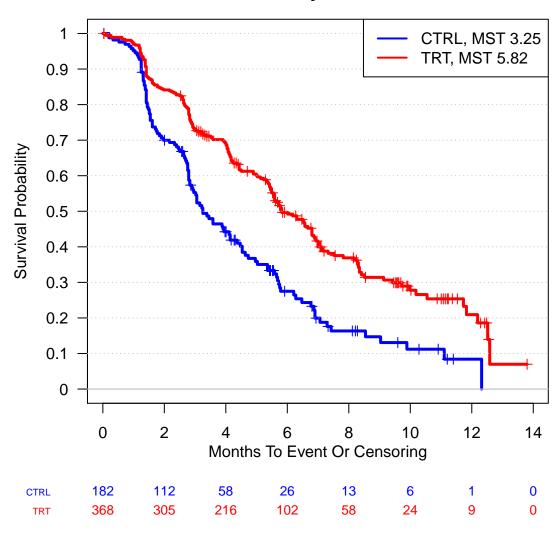
PFS BEP



[1] ""

By TRT

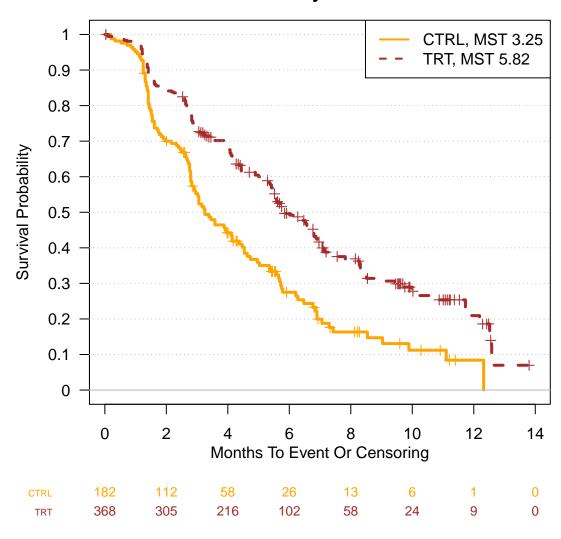
PFS ITT by treatment



[1] ""

By TRT, change color, line type

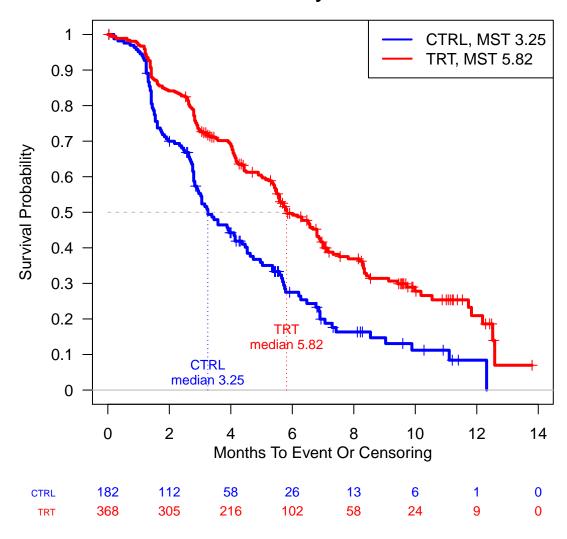
PFS ITT by treatment



[1] ""

Mark median PFS, no grid

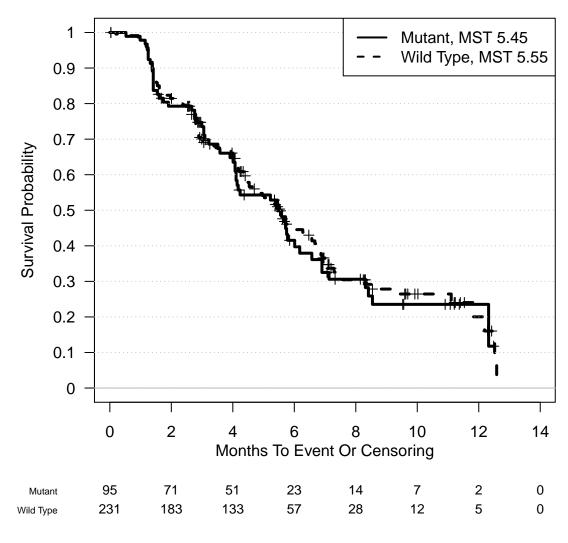
PFS ITT by treatment



[1] ""

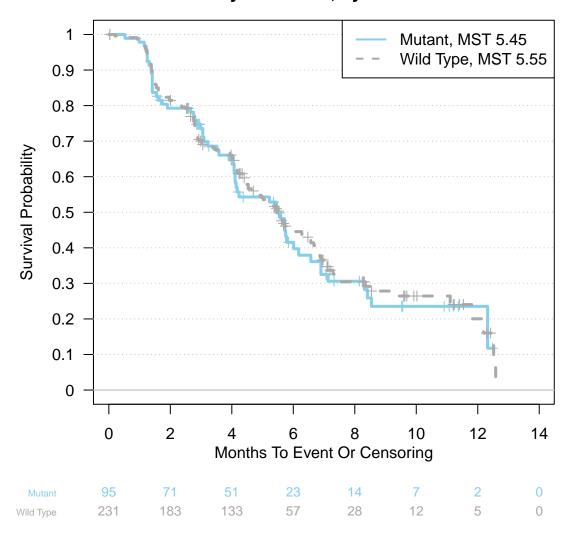
By KRAS.mutant only

OS BEP by treatment, by KRAS mutation



[1] ""

OS BEP by treatment, by KRAS mutation

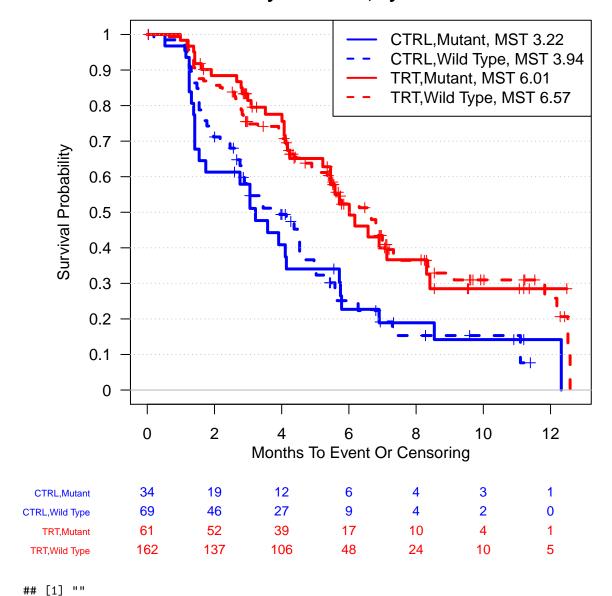


[1] ""

By TRT and KRAS.mutant

entries who have NA in trt, var, or varlist are removed

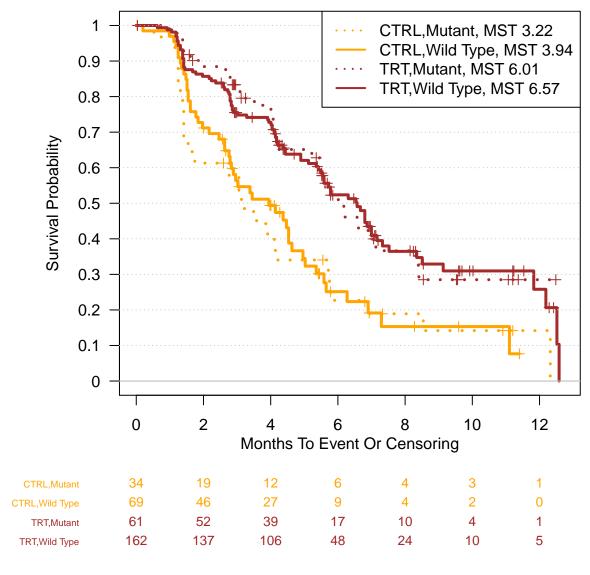
OS BEP by treatment, by KRAS mutation



By TRT and KRAS.mutant, change color and line type

entries who have NA in trt, var, or varlist are removed

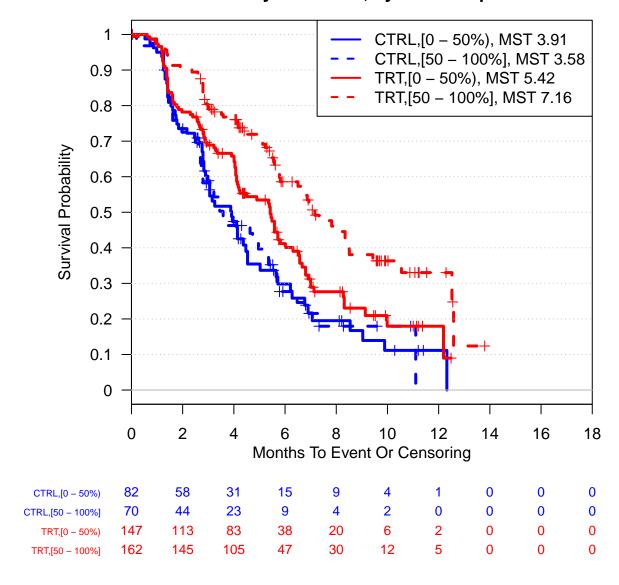
PFS BEP by treatment, by KRAS mutation



[1] ""

By TRT and KRAS.expression (continuous biomarker, cut at median)

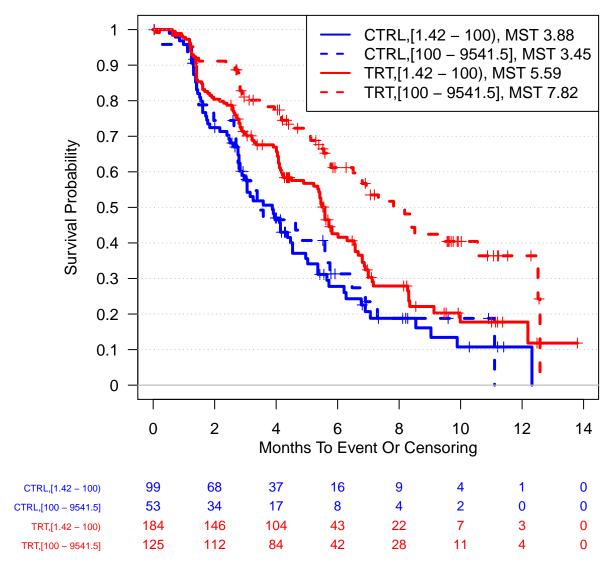
entries who have NA in trt, var, or varlist are removed



0%: 1.42. 50%: 70.52. 100%: 9541.5.

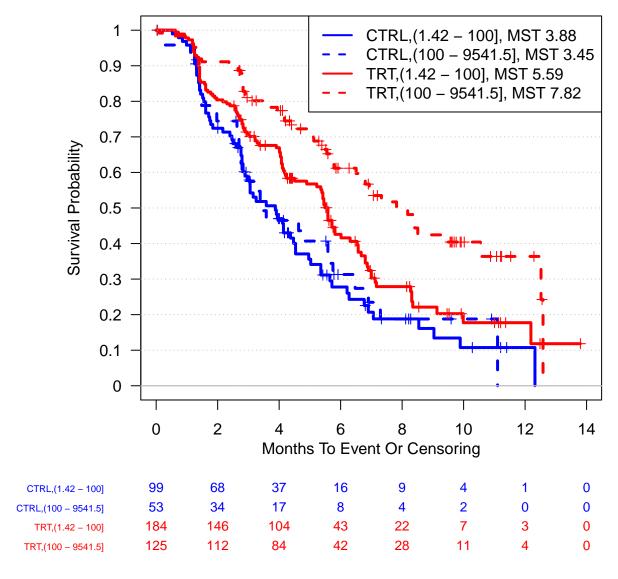
[1] ""

By TRT and KRAS.expression (continuous biomarker, cut at a numerical cutoff)



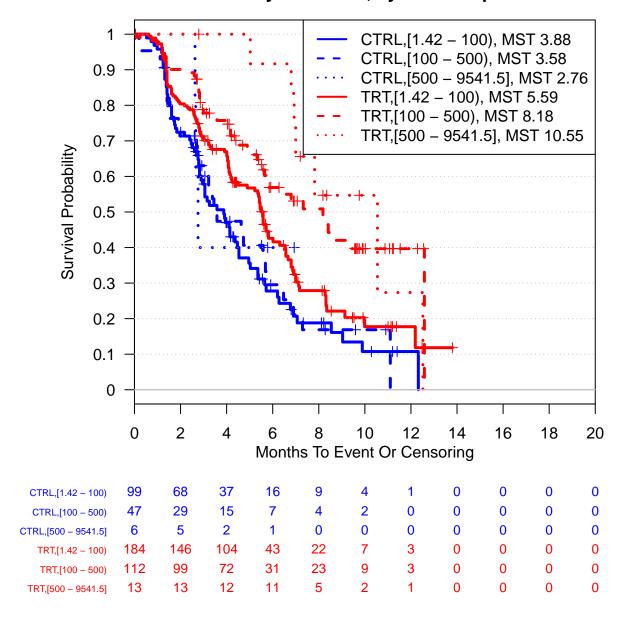
[1] ""

By TRT and KRAS.expression (continuous biomarker, cut at a numerical cutoff). High group defined as "greater than", instead of "greater than or equal to"



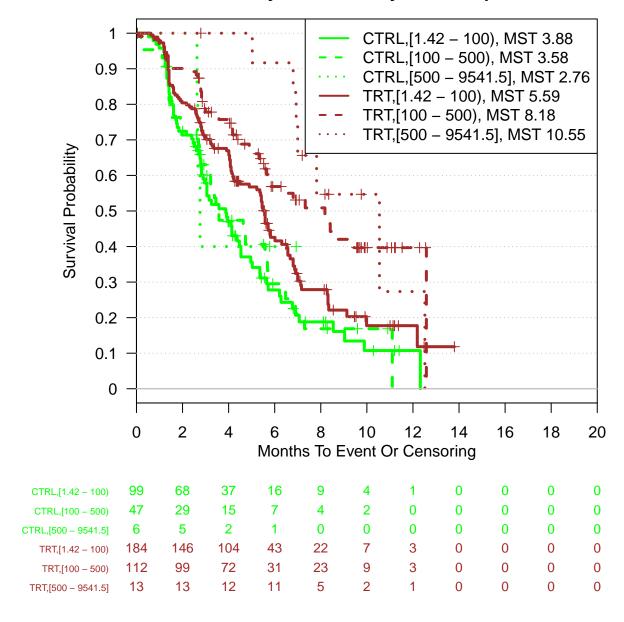
[1] ""

By TRT and KRAS.expression, more than 2 groups



[1] ""

PFS BEP by treatment, by KRAS expression



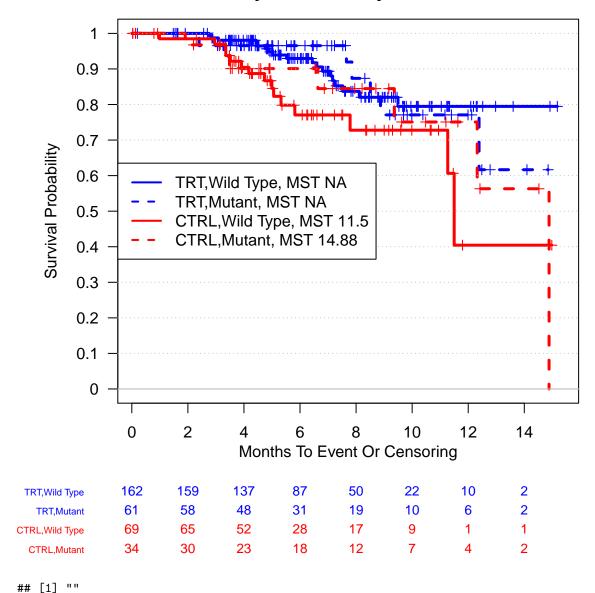
[1] ""

More flexibility, reorder subgroups

'varlist' is specified, trt and var parameters will be ignored

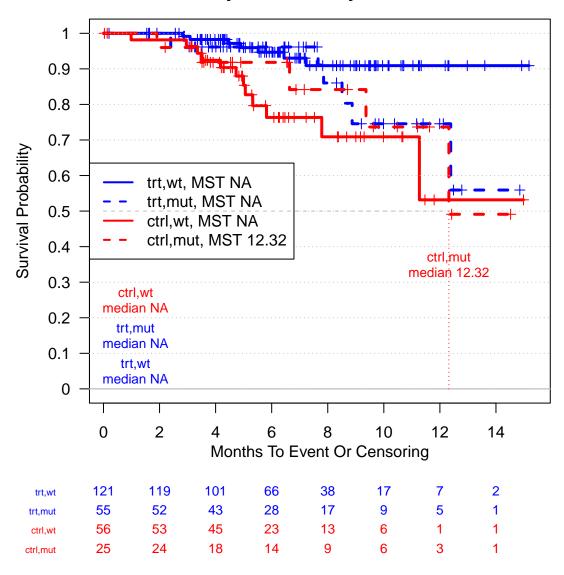
entries who have NA in trt, var, or varlist are removed

OS BEP by treatment, by KRAS mutation



By TRT and KRAS.mutant, reorder and rename

OS BEP by treatment, by KRAS mutation

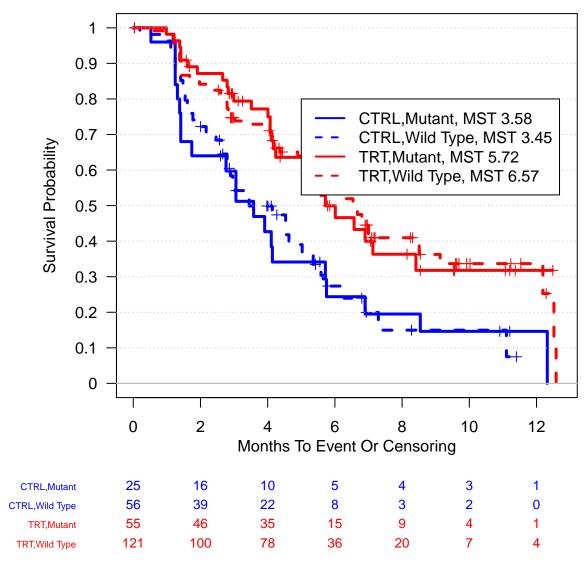


[1] ""

Legend location

more than one elements in 'var', trt parameter will be ignored

'varlist' is specified, trt and var parameters will be ignored



[1] ""

PlotTabForestBiomarker(): forest plot and summary statistics table for a single biomarker (include cutoff exploration for cont. biomarker)

Survival outcome, 2-arm, categorical variable

by default BEP will be defined as patients non-NA biomarker measurement

Across-arm Effect of Biomarker PFS, KRAS.mutant Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P		
All	CTRL	120 / 182	3.25					
	TRT	202 / 368	5.82	0.54	(0.43 – 0.67)	0.000000078	3 🛨	
BEP	CTRL	73 / 103	3.58					
	TRT	118 / 223	6.54	0.5	(0.37 – 0.66)	0.0000028	-	
KRAS.mutant(Mutant)	CTRL	26 / 34	3.22					
	TRT	31 / 61	6.01	0.48	(0.28 - 0.8)	0.0055		
KRAS.mutant(Wild Type)	CTRL	47 / 69	3.94					
	TRT	87 / 162	6.57	0.5	(0.35 – 0.72)	0.00019		
							0.28 1.0	0 1.89

0.28 1.0 1.89

--- TRT better [HR] CTRL be unadj P = 0.87(interaction

```
##
                                  code.v
##
    [1,] "Subgroup"
                                  "Group" "Event/N"
                                                       "MST" "HR"
   [2,] "All"
                                  "CTRL"
                                           "120 / 182" "3.25" ""
##
   [3,] ""
##
                                  "TRT"
                                           "202 / 368" "5.82" "0.54"
   [4,] "BEP"
                                  "CTRL"
                                          "73 / 103" "3.58" ""
##
   [5,] ""
                                           "118 / 223" "6.54" "0.5"
##
                                  "TRT"
                                           "26 / 34"
                                                       "3.22" ""
    [6,] "KRAS.mutant(Mutant)"
                                  "CTRL"
##
    [7,] ""
                                  "TRT"
                                           "31 / 61"
                                                       "6.01" "0.48"
##
                                                       "3.94" ""
##
    [8,] "KRAS.mutant(Wild Type)" "CTRL"
                                           "47 / 69"
##
    [9,] ""
                                   "TRT"
                                           "87 / 162" "6.57" "0.5"
##
##
   [1,] "CI"
                       "raw P"
   [2,] ""
##
   [3,] "0.43 - 0.67" "0.000000078"
##
##
    [4,] ""
##
   [5,] "0.37 - 0.66" "0.0000028"
   [6,] ""
   [7,] "0.28 - 0.8"
                       "0.0055"
##
   [8,] ""
##
## [9,] "0.35 - 0.72" "0.00019"
```

Survival outcome, another format

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker PFS, KRAS.mutant

Subgroup	Group	Event/N	MST	HR	CI	raw P	Fores	st plot
							TRT better	CTRL better
All	CTRL	120 / 182	3.25					1 1 1
	TRT	202 / 368	5.82	0.54	0.43 - 0.67	.00000007	-	
BEP	CTRL	73 / 103	3.58					i 1 1
	TRT	118 / 223	6.54	0.5	0.37 - 0.66	0.0000028	-	i
KRAS.mutant(Mutant)	CTRL	26 / 34	3.22					i 1 1
	TRT	31 / 61	6.01	0.48	0.28 - 0.8	0.0055 —	•	i
KRAS.mutant(Wild Type)	CTRL	47 / 69	3.94					i 1 1
	TRT	87 / 162	6.57	0.5	0.35 - 0.72	0.00019	-	i 1 1
unadj P = 0.87(interaction)	Unadjus	ted, unstratif	ied analy	/sis		0.28	0.53	1 1.89

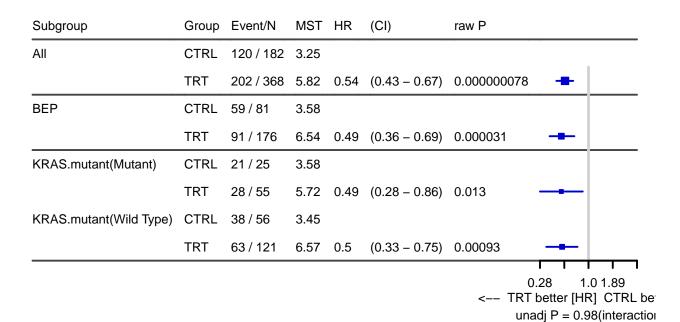
```
##
                                 code.v
## [1,] "Subgroup"
                                 "Group" "Event/N"
                                                     "MST" "HR"
                                 "CTRL" "120 / 182" "3.25" ""
## [2,] "All"
## [3,] ""
                                 "TRT"
                                         "202 / 368" "5.82" "0.54"
                                 "CTRL" "73 / 103" "3.58" ""
## [4,] "BEP"
## [5,] ""
                                 "TRT"
                                         "118 / 223" "6.54" "0.5"
   [6,] "KRAS.mutant(Mutant)"
                                 "CTRL"
                                         "26 / 34"
                                                     "3.22" ""
##
   [7,] ""
                                 "TRT"
                                         "31 / 61"
                                                    "6.01" "0.48"
##
                                                    "3.94" ""
  [8,] "KRAS.mutant(Wild Type)" "CTRL"
                                         "47 / 69"
##
   [9,] ""
                                 "TRT"
                                         "87 / 162" "6.57" "0.5"
##
##
## [1,] "CI"
                      "raw P"
## [2,] ""
## [3,] "0.43 - 0.67" "0.000000078"
##
   [4,] ""
## [5,] "0.37 - 0.66" "0.0000028"
## [6,] ""
## [7,] "0.28 - 0.8" "0.0055"
```

```
## [8,] "" ""
## [9,] "0.35 - 0.72" "0.00019"
```

Survival outcome, 2-arm, categorical variable, don't show ITT, BEP, rename variable name in display

user can also define BEP column

Across-arm Effect of Biomarker PFS, KRAS.mutant Unadjusted, unstratified analysis

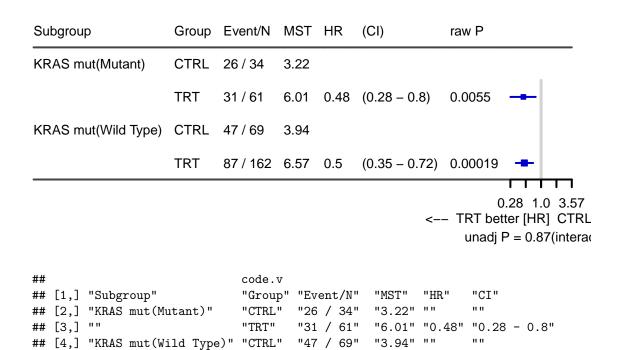


```
##
                                  code.v
                                  "Group" "Event/N"
                                                      "MST"
                                                            "HR"
##
   [1,] "Subgroup"
                                         "120 / 182" "3.25" ""
##
   [2,] "All"
                                  "CTRL"
   [3,] ""
                                  "TRT"
                                          "202 / 368" "5.82" "0.54"
##
                                                      "3.58" ""
##
   [4,] "BEP"
                                  "CTRL"
                                          "59 / 81"
  [5,] ""
                                  "TRT"
                                          "91 / 176"
                                                     "6.54" "0.49"
##
  [6,] "KRAS.mutant(Mutant)"
                                  "CTRL"
                                          "21 / 25"
                                                     "3.58" ""
                                  "TRT"
                                          "28 / 55"
                                                     "5.72" "0.49"
  [7,] ""
##
```

```
[8,] "KRAS.mutant(Wild Type)" "CTRL"
                                           "38 / 56"
##
    [9,] ""
                                   "TRT"
                                           "63 / 121" "6.57" "0.5"
##
   [1,] "CI"
                       "raw P"
##
##
    [2,] ""
   [3,] "0.43 - 0.67" "0.000000078"
##
   [4,] ""
##
   [5,] "0.36 - 0.69" "0.000031"
##
   [6,] ""
##
   [7,] "0.28 - 0.86" "0.013"
##
                       11 11
  [8,] ""
   [9,] "0.33 - 0.75" "0.00093"
##
PlotTabForestBiomarker(data=input,
                                   outcome.class="survival",
                                   outcome.var=c("PFS","PFS.event"),
                                   trt="Arm",
                                   var="KRAS.mutant",
                                   var.class="categorical",
                                   var.name="KRAS mut",
                                   show.itt=FALSE,
                                   show.bep=FALSE)
```

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker PFS, KRAS mut Unadjusted, unstratified analysis



```
## [5,] "" "TRT" "87 / 162" "6.57" "0.5" "0.35 - 0.72"
##
## [1,] "raw P"
## [2,] ""
## [3,] "0.0055"
## [4,] ""
## [5,] "0.00019"
```

Survival outcome, 2-arm, continuous variable, greater than some percentage cutoffs

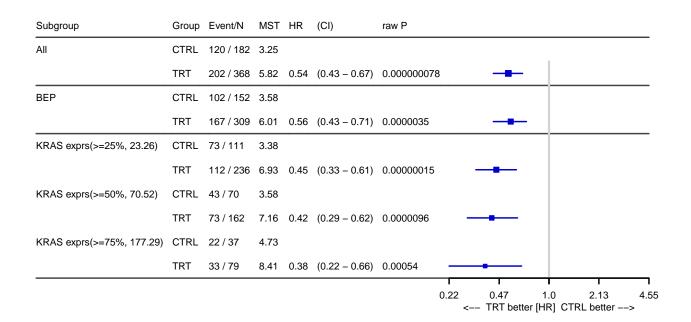
```
PlotTabForestBiomarker(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=c(.25,.5,.75),

# cols=c("black","black","darkgreen","darkgreen"),
numerical.cutoff=NULL,
greater=TRUE, less=FALSE,
within.bin=FALSE,
show.itt=TRUE, show.bep=TRUE)
```

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker PFS, KRAS exprs Unadjusted, unstratified analysis



```
##
                                    code.v
##
   [1,] "Subgroup"
                                    "Group" "Event/N" "MST" "HR"
                                    "CTRL"
   [2,] "All"
                                            "120 / 182" "3.25" ""
  [3,] ""
                                    "TRT"
                                            "202 / 368" "5.82" "0.54"
##
   [4,] "BEP"
                                            "102 / 152" "3.58" ""
##
                                    "CTRL"
##
  [5,] ""
                                    "TRT"
                                            "167 / 309" "6.01" "0.56"
  [6,] "KRAS exprs(>=25%, 23.26)"
                                    "CTRL"
                                            "73 / 111" "3.38" ""
   [7,] ""
                                            "112 / 236" "6.93" "0.45"
                                     "TRT"
##
##
   [8,] "KRAS exprs(>=50%, 70.52)"
                                    "CTRL"
                                            "43 / 70"
                                                         "3.58" ""
  [9,] ""
                                    "TRT"
                                            "73 / 162"
                                                        "7.16" "0.42"
## [10,] "KRAS exprs(>=75%, 177.29)" "CTRL"
                                            "22 / 37"
                                                        "4.73" ""
## [11,] ""
                                     "TRT"
                                            "33 / 79"
                                                        "8.41" "0.38"
##
##
   [1,] "CI"
                      "raw P"
  [2,] ""
##
   [3,] "0.43 - 0.67" "0.000000078"
##
##
  [4,] ""
  [5,] "0.43 - 0.71" "0.0000035"
## [6,] ""
## [7,] "0.33 - 0.61" "0.00000015"
## [8,] ""
## [9,] "0.29 - 0.62" "0.0000096"
## [10,] ""
## [11,] "0.22 - 0.66" "0.00054"
```

Survival outcome, 2-arm, continuous variable, less than some percentage cutoffs

```
PlotTabForestBiomarker(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=c(.25,.5,.75),
numerical.cutoff=NULL,
greater=FALSE, less=TRUE,
within.bin=FALSE,
show.itt=TRUE, show.bep=TRUE,
bep = 'BEP', bep.indicator=1)
```

Across-arm Effect of Biomarker PFS, KRAS exprs Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P							
All	CTRL	120 / 182	3.25										_
	TRT	202 / 368	5.82	0.54	(0.43 – 0.67)	0.000000078	8	_	-				
BEP	CTRL	59 / 81	3.58										
	TRT	91 / 176	6.54	0.49	(0.36 – 0.69)	0.000031		-					
KRAS exprs(<25%, 22.63)	CTRL	16 / 22	4.14										
	TRT	30 / 42	5.45	0.7	(0.37 – 1.32)	0.27	_			-			
KRAS exprs(<50%, 63.56)	CTRL	32 / 44	4.11										
	TRT	52 / 84	5.72	0.68	(0.43 – 1.06)	0.09		_	-		-		
KRAS exprs(<75%, 170.07)	CTRL	44 / 61	3.91										
	TRT	75 / 131	5.59	0.61	(0.42 – 0.89)	0.0098		_	-	-			
							0.36	<	0.60 TRT bett	1.0 er [HR		1.67 RL better>	2.78

```
##
                                     code.v
##
    [1,] "Subgroup"
                                     "Group" "Event/N"
                                                          "MST" "HR"
                                     "CTRL"
                                             "120 / 182" "3.25" ""
##
    [2,] "All"
                                             "202 / 368" "5.82" "0.54"
##
    [3,] ""
                                     "TRT"
    [4,] "BEP"
                                     "CTRL"
                                             "59 / 81"
                                                          "3.58" ""
##
##
    [5,] ""
                                     "TRT"
                                             "91 / 176" "6.54" "0.49"
                                     "CTRL"
                                             "16 / 22"
##
    [6,] "KRAS exprs(<25%, 22.63)"
                                                         "4.14" ""
    [7,] ""
                                     "TRT"
                                             "30 / 42"
                                                          "5.45" "0.7"
##
                                             "32 / 44"
                                                          "4.11" ""
##
    [8,] "KRAS exprs(<50%, 63.56)"
                                     "CTRL"
                                                         "5.72" "0.68"
##
    [9,] ""
                                     "TRT"
                                             "52 / 84"
                                             "44 / 61"
                                                          "3.91" ""
   [10,] "KRAS exprs(<75%, 170.07)" "CTRL"
                                     "TRT"
                                             "75 / 131"
                                                         "5.59" "0.61"
##
   [11,] ""
##
##
    [1,] "CI"
                       "raw P"
##
    [2,] ""
    [3,] "0.43 - 0.67" "0.000000078"
##
##
    [4,] ""
##
    [5,] "0.36 - 0.69" "0.000031"
   [6,] ""
   [7,] "0.37 - 1.32" "0.27"
##
##
   [8,] ""
  [9,] "0.43 - 1.06" "0.09"
##
## [10,] ""
## [11,] "0.42 - 0.89" "0.0098"
```

Survival outcome, 2-arm, continuous variable, greater and less than some percentage cutoffs

```
PlotTabForestBiomarker(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=c(.25,.5,.75),
numerical.cutoff=NULL,
greater=TRUE, less=TRUE,
within.bin=FALSE,
show.itt=TRUE, show.bep=TRUE)
```

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker PFS, KRAS exprs Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P	
All	CTRL	120 / 182	3.25				
	TRT	202 / 368	5.82	0.54	(0.43 - 0.67)	0.000000078	′8
BEP	CTRL	102 / 152	3.58				
	TRT	167 / 309	6.01	0.56	(0.43 - 0.71)	0.000035	
KRAS exprs(>=25%, 23.26)	CTRL	73 / 111	3.38				
	TRT	112 / 236	6.93	0.45	(0.33 – 0.61)	0.0000015	· -
KRAS exprs(>=50%, 70.52)	CTRL	43 / 70	3.58				
	TRT	73 / 162	7.16	0.42	(0.29 - 0.62)	0.0000096	
KRAS exprs(>=75%, 177.29)	CTRL	22 / 37	4.73				
	TRT	33 / 79	8.41	0.38	(0.22 - 0.66)	0.00054	
KRAS exprs(<25%, 23.26)	CTRL	29 / 41	3.94				
	TRT	55 / 73	4.07	1.04	(0.66 - 1.64)	0.87	
KRAS exprs(<50%, 70.52)	CTRL	59 / 82	3.91				
	TRT	94 / 147	5.42	0.73	(0.53 – 1.01)	0.06	
KRAS exprs(<75%, 177.29)	CTRL	80 / 115	3.58				
	TRT	134 / 230	5.59	0.63	(0.48 - 0.84)	0.0013	
							0.22 0.47 1.0 2.13 4.55 < TRT better [HR] CTRL better>

```
##
                                   code.v
##
   [1,] "Subgroup"
                                   "Group" "Event/N"
                                                      "MST"
## [2,] "All"
                                   "CTRL" "120 / 182" "3.25" ""
## [3,] ""
                                   "TRT"
                                           "202 / 368" "5.82" "0.54"
## [4,] "BEP"
                                          "102 / 152" "3.58" ""
                                   "CTRL"
                                   "TRT"
##
   [5,] ""
                                           "167 / 309" "6.01" "0.56"
                                           "73 / 111" "3.38" ""
## [6,] "KRAS exprs(>=25%, 23.26)" "CTRL"
## [7,] ""
                                   "TRT"
                                           "112 / 236" "6.93" "0.45"
## [8,] "KRAS exprs(>=50%, 70.52)" "CTRL" "43 / 70" "3.58" ""
```

```
## [9,] ""
                                    "TRT"
                                            "73 / 162" "7.16" "0.42"
## [10,] "KRAS exprs(>=75%, 177.29)" "CTRL"
                                            "22 / 37"
                                                        "4.73" ""
                                            "33 / 79"
## [11,] ""
                                    "TRT"
                                                        "8.41" "0.38"
                                                        "3.94" ""
## [12,] "KRAS exprs(<25%, 23.26)"
                                    "CTRL"
                                            "29 / 41"
                                            "55 / 73"
## [13,] ""
                                    "TRT"
                                                        "4.07" "1.04"
## [14,] "KRAS exprs(<50%, 70.52)"
                                    "CTRL" "59 / 82"
                                                        "3.91" ""
## [15,] ""
                                    "TRT"
                                            "94 / 147" "5.42" "0.73"
                                            "80 / 115" "3.58" ""
## [16,] "KRAS exprs(<75%, 177.29)"
                                    "CTRL"
## [17,] ""
                                    "TRT"
                                            "134 / 230" "5.59" "0.63"
##
## [1,] "CI"
                      "raw P"
## [2,] ""
## [3,] "0.43 - 0.67" "0.000000078"
## [4,] ""
## [5,] "0.43 - 0.71" "0.0000035"
   [6,] ""
##
## [7,] "0.33 - 0.61" "0.00000015"
## [8,] ""
## [9,] "0.29 - 0.62" "0.0000096"
## [10,] ""
## [11,] "0.22 - 0.66" "0.00054"
## [12,] ""
## [13,] "0.66 - 1.64" "0.87"
## [14.] ""
## [15,] "0.53 - 1.01" "0.06"
## [16,] ""
## [17,] "0.48 - 0.84" "0.0013"
```

"Less" rows next to "Greater" rows:

```
PlotTabForestBiomarker(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=c(.25,.5,.75),
numerical.cutoff=NULL,
greater=TRUE, less=TRUE, greater.by.less = TRUE,
within.bin=FALSE,
show.itt=TRUE, show.bep=TRUE)
```

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker PFS, KRAS exprs Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P	
All	CTRL	120 / 182	3.25				
	TRT	202 / 368	5.82	0.54	(0.43 - 0.67)	0.00000007	8 —
BEP	CTRL	102 / 152	3.58				
	TRT	167 / 309	6.01	0.56	(0.43 – 0.71)	0.0000035	
KRAS exprs(>=25%, 23.26)	CTRL	73 / 111	3.38				
	TRT	112 / 236	6.93	0.45	(0.33 – 0.61)	0.00000015	
KRAS exprs(<25%, 23.26)	CTRL	29 / 41	3.94				
	TRT	55 / 73	4.07	1.04	(0.66 - 1.64)	0.87	
KRAS exprs(>=50%, 70.52)	CTRL	43 / 70	3.58				
	TRT	73 / 162	7.16	0.42	(0.29 - 0.62)	0.0000096	
KRAS exprs(<50%, 70.52)	CTRL	59 / 82	3.91				
	TRT	94 / 147	5.42	0.73	(0.53 – 1.01)	0.06	
KRAS exprs(>=75%, 177.29)	CTRL	22 / 37	4.73				
	TRT	33 / 79	8.41	0.38	(0.22 - 0.66)	0.00054	
KRAS exprs(<75%, 177.29)	CTRL	80 / 115	3.58				
	TRT	134 / 230	5.59	0.63	(0.48 - 0.84)	0.0013	
							0.22

```
##
                                     code.v
    [1,] "Subgroup"
                                     "Group" "Event/N"
                                                          "MST" "HR"
##
                                             "120 / 182" "3.25" ""
##
    [2,] "All"
                                     "CTRL"
   [3,] ""
                                     "TRT"
                                              "202 / 368" "5.82" "0.54"
##
   [4,] "BEP"
                                              "102 / 152" "3.58" ""
##
                                      "CTRL"
    [5,] ""
                                     "TRT"
                                              "167 / 309" "6.01" "0.56"
##
                                     "CTRL"
                                             "73 / 111" "3.38" ""
##
   [6,] "KRAS exprs(>=25%, 23.26)"
                                     "TRT"
                                              "112 / 236" "6.93" "0.45"
##
   [7,] ""
                                              "29 / 41"
   [8,] "KRAS exprs(<25%, 23.26)"
                                      "CTRL"
                                                          "3.94" ""
##
                                              "55 / 73"
##
   [9,] ""
                                      "TRT"
                                                          "4.07" "1.04"
                                     "CTRL"
## [10,] "KRAS exprs(>=50%, 70.52)"
                                              "43 / 70"
                                                          "3.58" ""
## [11,] ""
                                      "TRT"
                                              "73 / 162"
                                                          "7.16" "0.42"
                                                          "3.91" ""
                                              "59 / 82"
## [12,] "KRAS exprs(<50%, 70.52)"
                                      "CTRL"
## [13,] ""
                                      "TRT"
                                              "94 / 147"
                                                          "5.42" "0.73"
## [14,] "KRAS exprs(>=75%, 177.29)" "CTRL"
                                             "22 / 37"
                                                          "4.73" ""
## [15,] ""
                                      "TRT"
                                              "33 / 79"
                                                          "8.41" "0.38"
## [16,] "KRAS exprs(<75%, 177.29)"
                                      "CTRL"
                                              "80 / 115" "3.58" ""
## [17,] ""
                                      "TRT"
                                              "134 / 230" "5.59" "0.63"
##
##
   [1,] "CI"
                       "raw P"
   [2,] ""
##
   [3,] "0.43 - 0.67" "0.00000078"
##
##
   [4,] ""
   [5,] "0.43 - 0.71" "0.0000035"
##
##
    [6,] ""
##
   [7,] "0.33 - 0.61" "0.00000015"
   [8,] ""
   [9,] "0.66 - 1.64" "0.87"
##
```

```
## [10,] "" ""
## [11,] "0.29 - 0.62" "0.0000096"
## [12,] "" ""
## [13,] "0.53 - 1.01" "0.06"
## [14,] "" ""
## [15,] "0.22 - 0.66" "0.00054"
## [16,] "" ""
## [17,] "0.48 - 0.84" "0.0013"
```

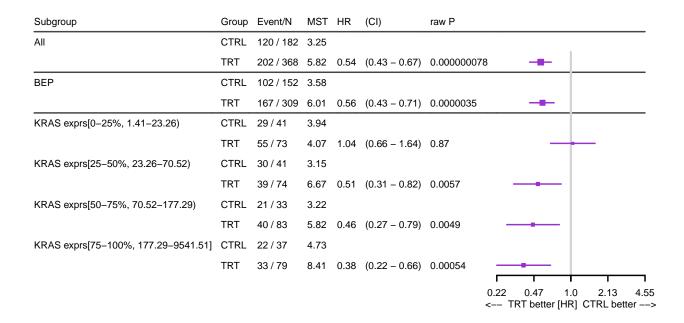
Survival outcome, 2-arm, continuous variable, within cutoff bin

```
PlotTabForestBiomarker(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=c(.25,.5,.75),
numerical.cutoff=NULL,
greater=FALSE, less=FALSE,
within.bin=TRUE,
show.itt=TRUE, show.bep=TRUE)
```

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker PFS, KRAS exprs Unadjusted, unstratified analysis



```
##
                                                code.v
                                                "Group" "Event/N"
## [1,] "Subgroup"
                                                                    "MST"
                                                "CTRL" "120 / 182" "3.25"
## [2,] "All"
## [3,] ""
                                                "TRT"
                                                        "202 / 368" "5.82"
   [4,] "BEP"
                                                        "102 / 152" "3.58"
##
                                                "CTRL"
## [5,] ""
                                                "TRT"
                                                        "167 / 309" "6.01"
## [6,] "KRAS exprs[0-25%, 1.41-23.26)"
                                                "CTRL"
                                                        "29 / 41"
                                                                     "3.94"
                                                        "55 / 73"
## [7,] ""
                                                "TRT"
                                                                     "4.07"
##
   [8,] "KRAS exprs[25-50%, 23.26-70.52)"
                                                "CTRL"
                                                        "30 / 41"
                                                                     "3.15"
  [9,] ""
##
                                                "TRT"
                                                        "39 / 74"
                                                                    "6.67"
## [10,] "KRAS exprs[50-75%, 70.52-177.29)"
                                                "CTRL"
                                                        "21 / 33"
                                                                     "3.22"
## [11,] ""
                                                "TRT"
                                                        "40 / 83"
                                                                     "5.82"
## [12,] "KRAS exprs[75-100%, 177.29-9541.51]" "CTRL"
                                                        "22 / 37"
                                                                    "4.73"
                                                "TRT"
                                                        "33 / 79"
## [13,] ""
                                                                    "8.41"
##
                "CI"
## [1,] "HR"
                              "raw P"
## [2,] ""
                11 11
                              11 11
## [3,] "0.54" "0.43 - 0.67" "0.000000078"
## [4,] ""
                11 11
## [5,] "0.56" "0.43 - 0.71" "0.0000035"
## [6,] ""
                11 11
## [7,] "1.04" "0.66 - 1.64" "0.87"
## [8,] ""
## [9,] "0.51" "0.31 - 0.82" "0.0057"
## [10,] ""
                11 11
## [11,] "0.46" "0.27 - 0.79" "0.0049"
## [12,] ""
## [13,] "0.38" "0.22 - 0.66" "0.00054"
```

Survival outcome, 2-arm, continuous variable, greater than some numerical cutoffs

```
PlotTabForestBiomarker(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=NULL,
numerical.cutoff=c(50,100),
greater=TRUE, less=FALSE,
within.bin=FALSE,
show.itt=TRUE, show.bep=TRUE)
```

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker PFS, KRAS exprs Unadjusted, unstratified analysis

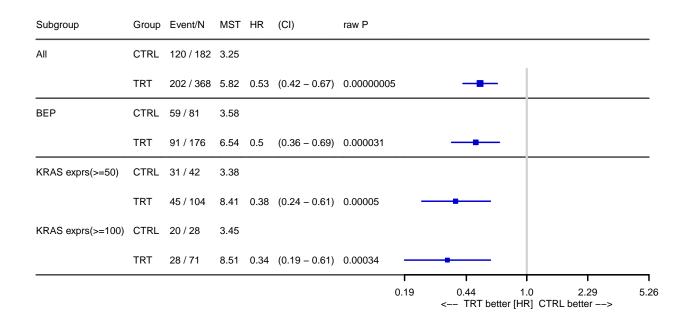
Subgroup	Group	Event/N	MST	HR	(CI)	raw P					
All	CTRL	120 / 182	3.25								
	TRT	202 / 368	5.82	0.54	(0.43 – 0.67)	0.00000007	8	-			
BEP	CTRL	102 / 152	3.58								
	TRT	167 / 309	6.01	0.56	(0.43 – 0.71)	0.0000035		-			
KRAS exprs(>=50)	CTRL	54 / 85	3.45								
	TRT	85 / 189	7.16	0.42	(0.3 – 0.6)	0.0000012	_	-			
KRAS exprs(>=100)	CTRL	32 / 53	3.45								
	TRT	56 / 125	7.82	0.42	(0.27 – 0.65)	0.00011		-			
							0.27	0.52 < TRT bette	1.0 er [HR]	1.92 etter>	3.7

```
##
                             code.v
##
    [1,] "Subgroup"
                             "Group" "Event/N"
                                                 "MST" "HR"
                                                                "CI"
   [2,] "All"
                             "CTRL" "120 / 182" "3.25" ""
##
   [3,] ""
                             "TRT"
                                     "202 / 368" "5.82" "0.54" "0.43 - 0.67"
##
   [4,] "BEP"
                             "CTRL" "102 / 152" "3.58" ""
                                                                11 11
##
    [5,] ""
                             "TRT"
                                     "167 / 309" "6.01" "0.56" "0.43 - 0.71"
##
                             "CTRL" "54 / 85"
                                                 "3.45" ""
##
   [6,] "KRAS exprs(>=50)"
                             "TRT"
                                     "85 / 189" "7.16" "0.42" "0.3 - 0.6"
##
   [7,] ""
                                     "32 / 53"
                                                 "3.45" ""
##
   [8,] "KRAS exprs(>=100)" "CTRL"
                                     "56 / 125" "7.82" "0.42" "0.27 - 0.65"
    [9,] ""
                             "TRT"
##
##
##
   [1,] "raw P"
   [2,] ""
##
##
    [3,] "0.000000078"
   [4,] ""
##
##
   [5,] "0.0000035"
   [6,] ""
##
##
   [7,] "0.0000012"
   [8,] ""
##
   [9,] "0.00011"
##
```

Survival outcome, 2-arm, continuous variable, adjust for covariates

```
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=NULL,
numerical.cutoff=c(50,100),
greater=TRUE, less=FALSE,
within.bin=FALSE,
show.itt=TRUE, show.bep=TRUE,
bep = 'BEP', bep.indicator=1, covariate="Age")
```

Across-arm Effect of Biomarker PFS, KRAS exprs Results adjusted by Age;



```
##
                              code.v
    [1,] "Subgroup"
                              "Group" "Event/N"
                                                   "MST" "HR"
                                                                  "CI"
    [2,] "All"
                              "CTRL"
                                      "120 / 182" "3.25" ""
##
    [3,] ""
                              "TRT"
##
                                      "202 / 368" "5.82" "0.53" "0.42 - 0.67"
    [4,] "BEP"
                              "CTRL"
                                      "59 / 81"
                                                   "3.58" ""
##
##
    [5,] ""
                              "TRT"
                                      "91 / 176"
                                                   "6.54" "0.5"
                                                                  "0.36 - 0.69"
    [6,] "KRAS exprs(>=50)"
                              "CTRL"
                                      "31 / 42"
                                                   "3.38" ""
##
##
    [7,] ""
                              "TRT"
                                       "45 / 104"
                                                   "8.41" "0.38" "0.24 - 0.61"
    [8,] "KRAS exprs(>=100)" "CTRL"
                                                   "3.45" ""
##
                                      "20 / 28"
##
    [9,] ""
                              "TRT"
                                      "28 / 71"
                                                   "8.51" "0.34" "0.19 - 0.61"
##
##
    [1,] "raw P"
##
   [2,] ""
   [3,] "0.00000005"
##
    [4,] ""
##
##
    [5,] "0.000031"
    [6,] ""
##
```

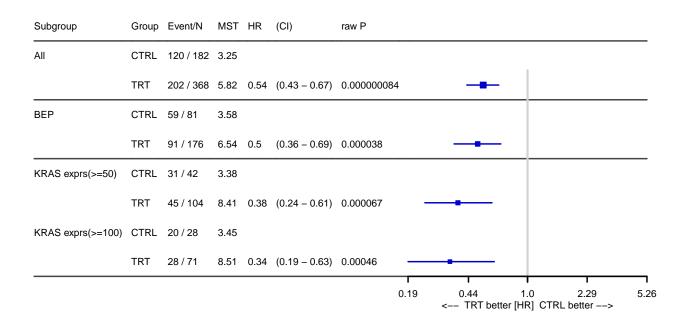
```
## [7,] "0.00005"
## [8,] ""
## [9,] "0.00034"
```

Survival outcome, 2-arm, continous variable, stratification

```
PlotTabForestBiomarker(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=NULL,
numerical.cutoff=c(50,100),
greater=TRUE, less=FALSE,
within.bin=FALSE,
show.itt=TRUE, show.bep=TRUE,
bep = 'BEP', bep.indicator=1, strata="Sex")
```

Across-arm Effect of Biomarker PFS, KRAS exprs ;Results stratified by Sex



```
##
                              code.v
                                                                  "CI"
##
    [1,] "Subgroup"
                              "Group" "Event/N"
                                                   "MST" "HR"
   [2,] "All"
                                                                  11 11
                              "CTRL"
                                       "120 / 182" "3.25" ""
##
                                       "202 / 368" "5.82" "0.54" "0.43 - 0.67"
##
    [3,] ""
                              "TRT"
   [4,] "BEP"
                                       "59 / 81"
                                                   "3.58" ""
##
                              "CTRL"
##
   [5,] ""
                              "TRT"
                                       "91 / 176"
                                                   "6.54" "0.5"
                                                                  "0.36 - 0.69"
                                       "31 / 42"
                                                   "3.38" ""
    [6,] "KRAS exprs(>=50)"
                              "CTRL"
##
```

```
[7,] ""
                            "TRT"
                                    "45 / 104" "8.41" "0.38" "0.24 - 0.61"
##
   [8,] "KRAS exprs(>=100)" "CTRL" "20 / 28"
                                               "3.45" ""
##
   [9,] ""
                            "TRT"
                                    "28 / 71"
                                               "8.51" "0.34" "0.19 - 0.63"
##
##
## [1,] "raw P"
## [2,] ""
## [3,] "0.000000084"
## [4,] ""
## [5,] "0.000038"
## [6,] ""
## [7,] "0.000067"
## [8,] ""
## [9,] "0.00046"
```

Survival outcome, 2-arm, continuous variable, adjust for covariates and stratified by strata

```
PlotTabForestBiomarker(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=NULL,
numerical.cutoff=c(50,100),
greater=TRUE, less=FALSE,
within.bin=FALSE,
show.itt=TRUE, show.bep=TRUE,
bep = 'BEP', bep.indicator=1,covariate="Age",strata="Sex")
```

Across-arm Effect of Biomarker PFS, KRAS exprs Results adjusted by Age;Results stratified by Sex

Subgroup	Group	Event/N	MST	HR	(CI)	raw P					
All	CTRL	120 / 182	3.25								
	TRT	202 / 368	5.82	0.53	(0.42 – 0.67)	0.00000005	3	_			
BEP	CTRL	59 / 81	3.58								
	TRT	91 / 176	6.54	0.5	(0.36 – 0.69)	0.000035		-			
KRAS exprs(>=50)	CTRL	31 / 42	3.38								
	TRT	45 / 104	8.41	0.39	(0.24 – 0.62)	0.000078	-	-			
KRAS exprs(>=100)	CTRL	20 / 28	3.45								
	TRT	28 / 71	8.51	0.34	(0.19 – 0.62)	0.00039		-			
							0.19	0.44 < TRT bet	1. ter [HR	2.29 better>	5.26

```
##
                              code.v
                                                                  "CI"
##
    [1,] "Subgroup"
                              "Group" "Event/N"
                                                   "MST" "HR"
                              "CTRL"
                                       "120 / 182" "3.25" ""
##
    [2,] "All"
##
    [3,] ""
                              "TRT"
                                       "202 / 368" "5.82" "0.53" "0.42 - 0.67"
                                       "59 / 81"
    [4,] "BEP"
                              "CTRL"
                                                   "3.58" ""
##
##
    [5,] ""
                              "TRT"
                                       "91 / 176"
                                                   "6.54" "0.5"
                                                                  "0.36 - 0.69"
                                                   "3.38" ""
                                      "31 / 42"
##
    [6,] "KRAS exprs(>=50)"
                              "CTRL"
    [7,] ""
                              "TRT"
                                       "45 / 104"
                                                   "8.41" "0.39" "0.24 - 0.62"
##
                                                   "3.45" ""
                                       "20 / 28"
                                                                  11 11
    [8,] "KRAS exprs(>=100)" "CTRL"
##
##
    [9,] ""
                              "TRT"
                                       "28 / 71"
                                                   "8.51" "0.34" "0.19 - 0.62"
##
##
    [1,] "raw P"
    [2,] ""
##
##
    [3,] "0.000000053"
##
   [4,] ""
    [5,] "0.000035"
##
##
    [6,] ""
##
    [7,] "0.000078"
    [8,] ""
    [9,] "0.00039"
##
```

Survival outcome, 1arm

within.bin, show.itt, show.bep will be ignored

only 1 arm; show.itt is set to FALSE ## only 1 arm; show.bep is set to FALSE

Within-arm Effect of Biomarker PFS, KRAS exprs Results adjusted by Age;Results stratified by Sex

Subgroup	Group	Event/N	MST	HR	(CI)	raw P	
KRAS exprs(>=50)	Less	82 / 120	5.39				
	Greater	85 / 189	7.16	0.54	(0.4 - 0.74)	0.000095	5 🗕
KRAS exprs(>=100)	Less	111 / 184	5.59				
	Greater	56 / 125	7.82	0.57	(0.41 – 0.78)	0.00062	-
							0.371.02.72
							HR

```
##
                            code.v
                                                                 "CI"
## [1,] "Subgroup"
                            "Group"
                                       "Event/N"
                                                   "MST" "HR"
## [2,] "KRAS exprs(>=50)"
                            "Less"
                                      "82 / 120" "5.39" ""
## [3,] ""
                            "Greater" "85 / 189" "7.16" "0.54" "0.4 - 0.74"
## [4,] "KRAS exprs(>=100)" "Less"
                                       "111 / 184" "5.59" ""
                            "Greater" "56 / 125" "7.82" "0.57" "0.41 - 0.78"
## [5,] ""
##
## [1,] "raw P"
## [2,] ""
## [3,] "0.000095"
## [4,] ""
## [5,] "0.00062"
```

Survival outcome, 2arm, flip TRT/CTRL order (calculate ctrl over trt HR)

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker PFS, KRAS exprs Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P					
All	TRT	202 / 368	5.82								
	CTRL	120 / 182	3.25	1.87	(1.49 – 2.34)	0.00000007	8			-	
BEP	TRT	167 / 309	6.01								
	CTRL	102 / 152	3.58	1.8	(1.4 – 2.3)	0.0000035				-	
KRAS exprs(>=25%, 23.26)	TRT	112 / 236	6.93								
	CTRL	73 / 111	3.38	2.23	(1.65 – 3)	0.00000015				-	-
KRAS exprs(>=50%, 70.52)	TRT	73 / 162	7.16								
	CTRL	43 / 70	3.58	2.37	(1.62 – 3.48)	0.0000096					_
KRAS exprs(>=75%, 177.29)	TRT	33 / 79	8.41								
	CTRL	22 / 37	4.73	2.64	(1.52 – 4.57)	0.00054					
							0.22	0.47 CTRL be	1. tter [H	2.14 TRT better	4.57 >

```
## code.v

## [1,] "Subgroup" "Group" "Event/N" "MST" "HR"

## [2,] "All" "TRT" "202 / 368" "5.82" ""

## [3,] "" "CTRL" "120 / 182" "3.25" "1.87"

## [4,] "BEP" "TRT" "167 / 309" "6.01" ""

## [5,] "" "CTRL" "102 / 152" "3.58" "1.8"
```

```
## [6,] "KRAS exprs(>=25%, 23.26)"
                                    "TRT"
                                            "112 / 236" "6.93" ""
## [7,] ""
                                    "CTRL"
                                            "73 / 111"
                                                        "3.38" "2.23"
## [8,] "KRAS exprs(>=50%, 70.52)"
                                            "73 / 162" "7.16" ""
                                    "TRT"
## [9,] ""
                                    "CTRL"
                                            "43 / 70"
                                                        "3.58" "2.37"
                                            "33 / 79"
                                                        "8.41" ""
## [10,] "KRAS exprs(>=75%, 177.29)" "TRT"
## [11,] ""
                                    "CTRL" "22 / 37" "4.73" "2.64"
## [1,] "CI"
                      "raw P"
##
   [2,] ""
## [3,] "1.49 - 2.34" "0.000000078"
                      11 11
## [4,] ""
## [5,] "1.4 - 2.3"
                      "0.000035"
## [6,] ""
                      "0.0000015"
## [7,] "1.65 - 3"
## [8,] ""
## [9,] "1.62 - 3.48" "0.0000096"
## [10,] ""
## [11,] "1.52 - 4.57" "0.00054"
```

Survival outcome, 2-arm, continuous variable, greater than some percentage cutoffs, show across-arm and within-arm results in the same plot

```
PlotTabForestBiomarker(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var="KRAS.exprs",
var.class="numeric", var.name="KRAS exprs",
percentile.cutoff=c(.25,.5,.75),
numerical.cutoff=NULL,
greater=TRUE, less=FALSE,
within.bin=FALSE,
show.itt=TRUE, show.bep=TRUE,
across.and.within = TRUE)
```

Some NAs in var column, will define the non NA entries as BEP

Across-arm and Within-arm Effect of Biomarker PFS, KRAS exprs Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P						
All	CTRL	120 / 182	3.25									
	TRT	202 / 368	5.82	0.54	(0.43 – 0.67)	0.00000007	8	-				
BEP	CTRL	102 / 152	3.58									_
	TRT	167 / 309	6.01	0.56	(0.43 – 0.71)	0.0000035		-	-			
KRAS exprs(>=25%, 23.26)	CTRL	73 / 111	3.38									
	TRT	112 / 236	6.93	0.45	(0.33 – 0.61)	0.00000015		-				
KRAS exprs(>=50%, 70.52)	CTRL	43 / 70	3.58									
	TRT	73 / 162	7.16	0.42	(0.29 – 0.62)	0.0000096		-				
KRAS exprs(>=75%, 177.29)	CTRL	22 / 37	4.73									
	TRT	33 / 79	8.41	0.38	(0.22 – 0.66)	0.00054	_	-				
CTRL:KRAS exprs(>=25%, 23.26)	Less	29 / 41	3.94									
	Greater	73 / 111	3.38	1.09	(0.7 – 1.68)	0.71			+			
CTRL:KRAS exprs(>=50%, 70.52)	Less	59 / 82	3.91									
	Greater	43 / 70	3.58	1	(0.67 – 1.48)	1			+	_		
CTRL:KRAS exprs(>=75%, 177.29)	Less	80 / 115	3.58									
	Greater	22 / 37	4.73	0.85	(0.53 – 1.37)	0.5			•	_		
TRT:KRAS exprs(>=25%, 23.26)	Less	55 / 73	4.07									_
	Greater	112 / 236	6.93	0.45	(0.33 – 0.63)	0.000002		-				
TRT:KRAS exprs(>=50%, 70.52)	Less	94 / 147	5.42									
	Greater	73 / 162	7.16	0.57	(0.42 – 0.78)	0.00043		-	-			
TRT:KRAS exprs(>=75%, 177.29)	Less	134 / 230	5.59									
	Greater	33 / 79	8.41	0.51	(0.35 – 0.75)	0.00061			-			
							0.22	0.47	1.0 HR	2.	13	4.55



```
[2,] "All"
                                                      "120 / 182" "3.25" ""
##
                                           "CTRL"
##
    [3,] ""
                                           "TRT"
                                                      "202 / 368" "5.82" "0.54"
                                                      "102 / 152" "3.58" ""
##
    [4,] "BEP"
                                           "CTRL"
   [5,] ""
                                           "TRT"
                                                      "167 / 309" "6.01" "0.56"
##
                                                                  "3.38" ""
##
    [6,] "KRAS exprs(>=25%, 23.26)"
                                           "CTRL"
                                                      "73 / 111"
   [7,] ""
                                           "TRT"
                                                      "112 / 236" "6.93" "0.45"
##
   [8,] "KRAS exprs(>=50%, 70.52)"
                                           "CTRL"
                                                      "43 / 70"
                                                                  "3.58" ""
                                                      "73 / 162"
                                                                  "7.16" "0.42"
   [9,] ""
                                           "TRT"
##
## [10,] "KRAS exprs(>=75%, 177.29)"
                                           "CTRL"
                                                      "22 / 37"
                                                                  "4.73" ""
  [11,] ""
                                           "TRT"
                                                      "33 / 79"
                                                                  "8.41" "0.38"
## [12,] "CTRL:KRAS exprs(>=25%, 23.26)"
                                           "Less"
                                                      "29 / 41"
                                                                  "3.94" ""
## [13,] ""
                                           "Greater" "73 / 111"
                                                                  "3.38" "1.09"
                                                      "59 / 82"
                                                                  "3.91" ""
## [14,] "CTRL:KRAS exprs(>=50%, 70.52)"
                                           "Less"
                                           "Greater" "43 / 70"
## [15,] ""
                                                                  "3.58" "1"
                                                      "80 / 115"
                                                                  "3.58" ""
## [16,] "CTRL:KRAS exprs(>=75%, 177.29)"
                                           "Less"
                                            "Greater" "22 / 37"
                                                                  "4.73" "0.85"
## [17,] ""
## [18,] "TRT:KRAS exprs(>=25%, 23.26)"
                                           "Less"
                                                      "55 / 73"
                                                                  "4.07" ""
                                           "Greater" "112 / 236" "6.93" "0.45"
## [19,] ""
                                                                  "5.42" ""
## [20,] "TRT:KRAS exprs(>=50%, 70.52)"
                                           "Less"
                                                      "94 / 147"
                                                                  "7.16" "0.57"
## [21,] ""
                                           "Greater" "73 / 162"
                                           "Less"
## [22,] "TRT:KRAS exprs(>=75%, 177.29)"
                                                      "134 / 230" "5.59" ""
## [23,] ""
                                           "Greater" "33 / 79"
                                                                  "8.41" "0.51"
##
    [1,] "CI"
##
                        "raw P"
   [2,] ""
##
   [3,] "0.43 - 0.67" "0.000000078"
   [4,] ""
##
    [5,] "0.43 - 0.71" "0.0000035"
##
   [6,] ""
##
   [7,] "0.33 - 0.61" "0.00000015"
##
   [8,] ""
##
   [9,] "0.29 - 0.62" "0.0000096"
##
## [10,] ""
## [11,] "0.22 - 0.66" "0.00054"
## [12,] ""
## [13,] "0.7 - 1.68"
                        "0.71"
## [14.] ""
## [15,] "0.67 - 1.48" "1"
## [16,] ""
## [17,] "0.53 - 1.37" "0.5"
## [18,] ""
## [19,] "0.33 - 0.63" "0.000002"
## [20.] ""
## [21,] "0.42 - 0.78" "0.00043"
## [22,] ""
## [23,] "0.35 - 0.75" "0.00061"
```

Response outcome, 2-arm, categorical variable

by default BEP will be defined as patients non-NA biomarker measurement

```
PlotTabForestBiomarker(data=input, outcome.class="binary",
```

```
outcome.var=c("Response"),
rsp.cat = TRUE,
rsp.response = c("CR","PR"),
rsp.nonresponse = c("SD", "PD","NON CR/PD","NE",NA),
trt="Arm",
var="KRAS.mutant",
var.class="categorical")
```

Covariate adjustment and stratification are not supported for binary outcome

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker Response, KRAS.mutant Unadjusted, unstratified analysis

Subgroup	Group	nRsp/N	Rsp Rate	deltaRR	(CI)	raw P	
All	CTRL	14 / 182	0.08				
	TRT	96 / 368	0.26	0.18	(0.12 – 0.25)	0.0000007	•
BEP	CTRL	11 / 103	0.11				
	TRT	54 / 223	0.24	0.14	(0.05 – 0.22)	0.007	-
KRAS.mutant(Mutant)	CTRL	5 / 34	0.15				
	TRT	18 / 61	0.3	0.15	(-0.04 - 0.34)	0.17	-
KRAS.mutant(Wild Type)	CTRL	6 / 69	0.09				
	TRT	36 / 162	0.22	0.14	(0.03 – 0.24)	0.024	-

-0.34 0 0.34 <-- CTRL better [deltaRR] TF * Unadj P = 0.77 (intera

```
##
                                   code.v
                                                       "Rsp Rate" "deltaRR"
##
    [1,] "Subgroup"
                                   "Group" "nRsp/N"
                                            "14 / 182" "0.08"
    [2,] "All"
##
                                   "CTRL"
   [3,] ""
                                   "TRT"
                                            "96 / 368" "0.26"
                                                                   "0.18"
##
   [4,] "BEP"
                                   "CTRL"
                                            "11 / 103" "0.11"
                                                                   11 11
##
    [5,] ""
                                            "54 / 223" "0.24"
                                                                   "0.14"
##
                                   "TRT"
   [6,] "KRAS.mutant(Mutant)"
                                   "CTRL"
                                           "5 / 34"
                                                       "0.15"
                                                                   11 11
##
                                   "TRT"
                                            "18 / 61" "0.3"
                                                                   "0.15"
   [7,] ""
                                            "6 / 69"
                                                                   11 11
   [8,] "KRAS.mutant(Wild Type)" "CTRL"
                                                       "0.09"
##
                                                                   "0.14"
##
   [9,] ""
                                   "TRT"
                                            "36 / 162" "0.22"
##
## [1,] "CI"
                         "raw P"
## [2,] ""
```

```
## [3,] "0.12 - 0.25" "0.0000007"

## [4,] "" ""

## [5,] "0.05 - 0.22" "0.007"

## [6,] "" ""

## [7,] "-0.04 - 0.34" "0.17"

## [8,] "" ""

## [9,] "0.03 - 0.24" "0.024"
```

Response outcome, another format

```
PlotTabForestBiomarker(data=input,

outcome.class="binary",
outcome.var=c("Response"),
rsp.cat = TRUE,
rsp.response = c("CR","PR"),
rsp.nonresponse = c("SD", "PD","NON CR/PD","NE",NA),
trt="Arm",
var="KRAS.mutant",
var.class="categorical",
tabforest = TRUE)
```

- ## Covariate adjustment and stratification are not supported for binary outcome
- ## Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker Response, KRAS.mutant

Subgroup	Group	nRsp/N	Rsp Rate	deltaRR	CI	raw P	F	orest plo	ot	
							CTRL better		TRT better	
All	CTRL	14 / 182	0.08							
	TRT	96 / 368	0.26	0.18	0.12 – 0.25	0.0000007			-	
BEP	CTRL	11 / 103	0.11							
	TRT	54 / 223	0.24	0.14	0.05 - 0.22	0.007		_	•	
KRAS.mutant(Mutant)	CTRL	5 / 34	0.15							
	TRT	18 / 61	0.3	0.15	-0.04 - 0.34	0.17			•	
KRAS.mutant(Wild Type)	CTRL	6 / 69	0.09							
	TRT	36 / 162	0.22	0.14	0.03 - 0.24	0.024		_	•	
Unadj P = 0.77 (interaction)	Unadjus	ted, unstrat	ified analy	sis		-0.3	1 4 –0.17	0	0.17	0.3

```
## code.v
## [1,] "Subgroup" "Group" "nRsp/N" "Rsp Rate" "deltaRR"
## [2,] "All" "CTRL" "14 / 182" "0.08" ""
## [3,] "" "TRT" "96 / 368" "0.26" "0.18"
```

```
11 11
## [4,] "BEP"
                                  "CTRL"
                                          "11 / 103" "0.11"
   [5,] ""
                                  "TRT"
##
                                          "54 / 223" "0.24"
                                                                 "0.14"
   [6,] "KRAS.mutant(Mutant)"
                                                                 11 11
                                          "5 / 34"
                                                      "0.15"
                                  "CTRL"
                                                                 "0.15"
  [7,] ""
                                  "TRT"
                                          "18 / 61" "0.3"
##
                                                                 11 11
   [8,] "KRAS.mutant(Wild Type)" "CTRL"
##
                                          "6 / 69"
                                                      "0.09"
##
   [9,] ""
                                  "TRT"
                                          "36 / 162" "0.22"
                                                                 "0.14"
## [1,] "CI"
                        "raw P"
##
   [2,] ""
## [3,] "0.12 - 0.25" "0.0000007"
                        11 11
## [4,] ""
## [5,] "0.05 - 0.22"
                       "0.007"
                        11 11
## [6,] ""
## [7,] "-0.04 - 0.34" "0.17"
## [8,] ""
                        11 11
## [9,] "0.03 - 0.24" "0.024"
```

Continuous outcome, 2-arm, categorical variable

```
PlotTabForestBiomarker(data=input,

outcome.class="continuous",
outcome.var=c("Lab_ontrt"),
trt="Arm",
var="KRAS.mutant",
var.class="categorical")
```

Stratification is not supported for continuous outcome

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker Lab_ontrt, KRAS.mutant Unadjusted, unstratified analysis

Subgroup	Group	Mean	delta	(CI)	raw P
All	CTRL	19.22			_
	TRT	22.17	2.95	(1.64 – 4.26)	0.000012
BEP	CTRL	19.67			
	TRT	22.42	2.75	(1.06 – 4.44)	0.0015
KRAS.mutant(Mutant)	CTRL	19.54			
	TRT	23.22	3.68	(0.56 - 6.8)	0.021
KRAS.mutant(Wild Type)	CTRL	19.73			
	TRT	22.11	2.38	(0.36 – 4.41)	0.021
					-6.8 -3.4 0 3.4 6.8
					<pre>-0.0 -3.4 0 3.4 6.0 < CTRL better [delta] TRT better</pre>
					* Unadj P = 0.48 interaction

```
##
                                 code.v
                                 "Group" "Mean" "delta" "CI"
## [1,] "Subgroup"
## [2,] "All"
                                 "CTRL" "19.22" ""
                                                         11 11
## [3,] ""
                                 "TRT"
                                         "22.17" "2.95" "1.64 - 4.26"
                                                         11 11
   [4,] "BEP"
                                 "CTRL"
                                         "19.67" ""
##
  [5,] ""
                                 "TRT"
                                         "22.42" "2.75"
                                                         "1.06 - 4.44"
##
  [6,] "KRAS.mutant(Mutant)"
                                 "CTRL"
                                         "19.54" ""
  [7,] ""
                                         "23.22" "3.68"
                                                         "0.56 - 6.8"
##
                                 "TRT"
   [8,] "KRAS.mutant(Wild Type)" "CTRL" "19.73" ""
                                                         11 11
##
## [9,] ""
                                 "TRT"
                                         "22.11" "2.38" "0.36 - 4.41"
## [1,] "raw P"
## [2,] ""
## [3,] "0.000012"
## [4,] ""
## [5,] "0.0015"
## [6,] ""
## [7,] "0.021"
## [8,] ""
## [9,] "0.021"
```

var.class="categorical",tabforest=T)

Stratification is not supported for continuous outcome

Some NAs in var column, will define the non NA entries as BEP

Across-arm Effect of Biomarker Lab_ontrt, KRAS.mutant

Subgroup	Group	Mean	delta	CI	raw P	Forest plot		
						CTRL better	TRT better	
All	CTRL	19.22					1	
	TRT	22.17	2.95	1.64 – 4.26	0.000012			
BEP	CTRL	19.67						
	TRT	22.42	2.75	1.06 – 4.44	0.0015		•	
KRAS.mutant(Mutant)	CTRL	19.54						
	TRT	23.22	3.68	0.56 - 6.8	0.021		•	
KRAS.mutant(Wild Type)	CTRL	19.73						
	TRT	22.11	2.38	0.36 – 4.41	0.021		•	
* Unadj P = 0.48 interaction	8 Interaction Unadjusted, unstratified analysis						0 3.4 6.8	

```
##
                                  code.v
##
   [1,] "Subgroup"
                                  "Group" "Mean" "delta" "CI"
##
   [2,] "All"
                                  "CTRL"
                                          "19.22" ""
                                                           11 11
   [3,] ""
                                  "TRT"
                                          "22.17" "2.95" "1.64 - 4.26"
##
   [4,] "BEP"
                                  "CTRL"
                                          "19.67" ""
                                                           11 11
##
   [5,] ""
                                          "22.42" "2.75"
                                  "TRT"
                                                           "1.06 - 4.44"
##
   [6,] "KRAS.mutant(Mutant)"
                                  "CTRL" "19.54" ""
                                                           11 11
##
   [7,] ""
                                  "TRT"
                                          "23.22" "3.68"
                                                           "0.56 - 6.8"
##
##
   [8,] "KRAS.mutant(Wild Type)" "CTRL"
                                          "19.73" ""
    [9,] ""
                                   "TRT"
                                          "22.11" "2.38"
                                                           "0.36 - 4.41"
##
##
   [1,] "raw P"
##
   [2,] ""
##
   [3,] "0.000012"
##
   [4,] ""
##
##
   [5,] "0.0015"
   [6,] ""
##
## [7,] "0.021"
## [8,] ""
## [9,] "0.021"
```

PlotTabForestMulti(): Forest plots to compare multiple variates' effect in ITT vs BEP, or compare multiple variates' effect in subpopulations

2-arm, compare BEP vs ITT

Across arm, Compare BEP vs. All PFS Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P	
ITT Sex(F)	CTRL	57 / 89	3.38				
	TRT	105 / 184	5.72	0.54	(0.39 – 0.74)	0.00018	-
BEP Sex(F)	CTRL	28 / 39	4.14				
	TRT	52 / 90	5.49	0.58	(0.36 – 0.92)	0.021	
ITT Sex(M)	CTRL	63 / 93	3.22				
	TRT	97 / 184	6.54	0.54	(0.39 – 0.74)	0.00012	-
BEP Sex(M)	CTRL	31 / 42	3.02				
	TRT	39 / 86	6.8	0.42	(0.26 – 0.68)	0.00043	
ITT Age(>=50%, 53)	CTRL	56 / 80	3.06				
	TRT	120 / 207	5.59	0.56	(0.41 – 0.77)	0.00035	
BEP Age(>=50%, 54)	CTRL	26 / 36	3.38				
	TRT	53 / 93	5.72	0.63	(0.39 – 1.01)	0.053	
ITT Age(<50%, 53)	CTRL	64 / 102	3.94				
	TRT	82 / 161	6.8	0.48	(0.35 – 0.67)	0.000019	-
BEP Age(<50%, 54)	CTRL	33 / 45	3.91				
	TRT	38 / 83	6.8	0.37	(0.23 – 0.6)	0.000048	
							0 0.5 1 - TRT better [HR] CTRL better:

2-arm, compare subgroups defined by biomarker

```
PlotTabForestMulti(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var=c("Sex","Age"),
bep="BEP",bep.indicator=1, compare.bep.itt=FALSE,
compare.subgroup=TRUE, subgroup="KRAS.mutant"
)
```

Across arm, Compare KRAS.mutant subgroup PFS Unadjusted, unstratified analysis

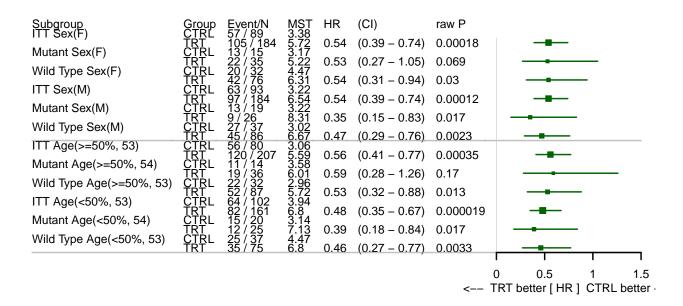
Subgroup Group Event/N MST HR (CI) raw P Mutant Sex(F) CTRL 13 / 15 3.17 TRT 22 / 35 5.22 0.53 (0.27 - 1.05) 0.069 Wild Type Sex(F) CTRL 20/32 4.47 $0.54 \quad (0.31 - 0.94) \quad 0.03$ TRT 42 / 76 6.31 Mutant Sex(M) CTRL 13 / 19 3.22 TRT 9/26 8.31 $0.35 \quad (0.15 - 0.83) \quad 0.017$ Wild Type Sex(M) CTRL 27 / 37 3.02 45 / 86 $0.47 \quad (0.29 - 0.76) \quad 0.0023$ TRT 6.67 Mutant Age(>=50%, 54) CTRL 11 / 14 3.58 TRT 19/36 6.01 0.59 (0.28 - 1.26) 0.17 CTRL 22/32 Wild Type Age(>=50%, 53) 2.96 52 / 87 5.72 0.53 (0.32 - 0.88) 0.013 TRT Mutant Age(<50%, 54) CTRL 15/20 3.14 12 / 25 7.13 0.39 (0.18 - 0.84) 0.017 TRT Wild Type Age(<50%, 53) CTRL 25/37 4.47 TRT 35 / 75 6.8 0.46 (0.27 - 0.77) 0.0033 0 0.5 1.5 <-- TRT better [HR] CTRL better --

$2\text{-}\mathrm{arm},$ compare subgroups defined by biomarker, also show ITT

```
PlotTabForestMulti(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm",
var=c("Sex","Age"),
bep="BEP",bep.indicator=1, compare.bep.itt=FALSE,
compare.subgroup=TRUE, subgroup="KRAS.mutant", show.itt=TRUE)
```

Across arm, Compare KRAS.mutant subgroup PFS Unadjusted, unstratified analysis



2-arm, compare subgroups defined by biomarker, also show BEP

Across arm, Compare KRAS.mutant subgroup PFS Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P	
ITT Sex(F)	CTRL	57 / 89	3.38				_
	TRT	105 / 184	5.72	0.54	(0.39 - 0.74)	0.00018	-
BEP Sex(F)	CTRL	28 / 39	4.14				
	TRT	52 / 90	5.49	0.58	(0.36 - 0.92)	0.021	
Mutant Sex(F)	CTRL	13 / 15	3.17				
	TRT	22 / 35	5.22	0.53	(0.27 - 1.05)	0.069	_
Wild Type Sex(F)	CTRL	20 / 32	4.47				
	TRT	42 / 76	6.31	0.54	(0.31 – 0.94)	0.03	_
ITT Sex(M)	CTRL	63 / 93	3.22				
	TRT	97 / 184	6.54	0.54	(0.39 - 0.74)	0.00012	-
BEP Sex(M)	CTRL	31 / 42	3.02				
	TRT	39 / 86	6.8	0.42	(0.26 - 0.68)	0.00043	_
Mutant Sex(M)	CTRL	13 / 19	3.22				
	TRT	9 / 26	8.31	0.35	(0.15 - 0.83)	0.017	
Wild Type Sex(M)	CTRL	27 / 37	3.02				
	TRT	45 / 86	6.67	0.47	(0.29 - 0.76)	0.0023	-
ITT Age(>=50%, 53)	CTRL	56 / 80	3.06				
	TRT	120 / 207	5.59	0.56	(0.41 – 0.77)	0.00035	-
BEP Age(>=50%, 54)	CTRL	26 / 36	3.38				
	TRT	53 / 93	5.72	0.63	(0.39 – 1.01)	0.053	
Mutant Age(>=50%, 54)	CTRL	11 / 14	3.58				
	TRT	19 / 36	6.01	0.59	(0.28 – 1.26)	0.17	
Wild Type Age(>=50%, 53)	CTRL	22 / 32	2.96				
	TRT	52 / 87	5.72	0.53	(0.32 - 0.88)	0.013	_
ITT Age(<50%, 53)	CTRL	64 / 102	3.94				
	TRT	82 / 161	6.8	0.48	(0.35 - 0.67)	0.000019	-
BEP Age(<50%, 54)	CTRL	33 / 45	3.91				
	TRT	38 / 83	6.8	0.37	(0.23 - 0.6)	0.000048	-
Mutant Age(<50%, 54)	CTRL	15 / 20	3.14				
	TRT	12 / 25	7.13	0.39	(0.18 - 0.84)	0.017	
Wild Type Age(<50%, 53)	CTRL	25 / 37	4.47		. ,		
,, J. (),,	TRT	35 / 75	6.8	0.46	(0.27 - 0.77)	0.0033	-
					. ,		
							0 0.5 1 1.5 FRT better [HR] CTRL better
						ζ Ι	KI Detter [TIK] CTKE Detter.

If bep column is not defined, the program will take the non NA entries in subgroups column as BEP

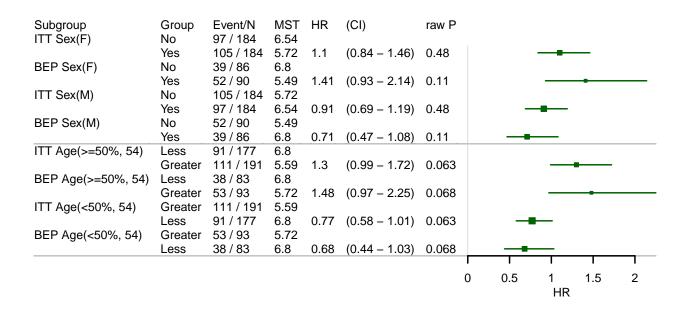
show.bep is TRUE but bep is not specified, will define the non NA entries in subgroup column as BEP

Across arm, Compare KRAS.mutant subgroup PFS Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P	
ITT Sex(F)	CTRL	57 / 89	3.38				
	TRT	105 / 184	5.72	0.54	(0.39 - 0.74)	0.00018	-
BEP Sex(F)	CTRL	33 / 47	4.11				
	TRT	64 / 111	5.59	0.53	(0.35 - 0.81)	0.0037	-
Mutant Sex(F)	CTRL	13 / 15	3.17				
	TRT	22 / 35	5.22	0.53	(0.27 – 1.05)	0.069	
Wild Type Sex(F)	CTRL	20 / 32	4.47				
	TRT	42 / 76	6.31	0.54	(0.31 – 0.94)	0.03	-
ITT Sex(M)	CTRL	63 / 93	3.22				
	TRT	97 / 184	6.54	0.54	(0.39 - 0.74)	0.00012	-
BEP Sex(M)	CTRL	40 / 56	3.06				
	TRT	54 / 112	6.8	0.46	(0.3 - 0.7)	0.00024	-
Mutant Sex(M)	CTRL	13 / 19	3.22				
	TRT	9 / 26	8.31	0.35	(0.15 – 0.83)	0.017	-
Wild Type Sex(M)	CTRL	27 / 37	3.02				
	TRT	45 / 86	6.67	0.47	(0.29 - 0.76)	0.0023	-
ITT Age(>=50%, 53)	CTRL	56 / 80	3.06				
	TRT	120 / 207	5.59	0.56	(0.41 – 0.77)	0.00035	-
BEP Age(>=50%, 53)	CTRL	34 / 47	3.02				
	TRT	71 / 123	6.01	0.52	(0.34 - 0.79)	0.0019	-
Mutant Age(>=50%, 54)	CTRL	11 / 14	3.58				
	TRT	19 / 36	6.01	0.59	(0.28 – 1.26)	0.17	
Wild Type Age(>=50%, 53)	CTRL	22 / 32	2.96				
	TRT	52 / 87	5.72	0.53	(0.32 - 0.88)	0.013	-
ITT Age(<50%, 53)	CTRL	64 / 102	3.94				
	TRT	82 / 161	6.8	0.48	(0.35 - 0.67)	0.000019	-
BEP Age(<50%, 53)	CTRL	39 / 56	4.11				_
	TRT	47 / 100	6.8	0.44	(0.29 - 0.67)	0.00017	-
Mutant Age(<50%, 54)	CTRL	15 / 20	3.14				
	TRT	12 / 25	7.13	0.39	(0.18 - 0.84)	0.017	_
Wild Type Age(<50%, 53)	CTRL	25 / 37	4.47				
	TRT	35 / 75	6.8	0.46	(0.27 - 0.77)	0.0033	-
							0 05 4 45
							0 0.5 1 1.5 FRT better [HR] CTRL better
						7	

1-arm, compare ITT vs BEP

Within arm, Compare BEP vs. All PFS Unadjusted, unstratified analysis



2-arm, compare subgroups defined by biomarker, multiple cutoffs for continuous biomarker

Across arm, Compare KRAS.mutant subgroup PFS Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P	
Mutant Sex(F)	CTRL	13 / 15	3.17				
	TRT	22 / 35	5.22	0.53	(0.27 – 1.05)	0.069	_
Wild Type Sex(F)	CTRL	20 / 32	4.47				
	TRT	42 / 76	6.31	0.54	(0.31 – 0.94)	0.03	-
Mutant Sex(M)	CTRL	13 / 19	3.22				
	TRT	9 / 26	8.31	0.35	(0.15 – 0.83)	0.017	-
Wild Type Sex(M)	CTRL	27 / 37	3.02				
	TRT	45 / 86	6.67	0.47	(0.29 – 0.76)	0.0023	-
Mutant Age(>=33%, 49)	CTRL	19 / 22	3.06				
	TRT	23 / 42	5.59	0.53	(0.29 – 0.98)	0.043	-
Wild Type Age(>=33%, 48)	CTRL	30 / 44	3.94				
	TRT	61 / 111	6.31	0.49	(0.31 – 0.76)	0.0017	-
Mutant Age(>=66%, 59)	CTRL	7/9	5.78				
	TRT	13 / 25	6.18	0.87	(0.32 – 2.38)	0.79	
Wild Type Age(>=66%, 58)	CTRL	16 / 25	3.38				
	TRT	35 / 57	5.49	0.63	(0.35 – 1.16)	0.14	-
Mutant Age(<33%, 49)	CTRL	7 / 12	3.56				
	TRT	8 / 19	8.31	0.4	(0.15 – 1.13)	0.083	-
Wild Type Age(<33%, 48)	CTRL	17 / 25	4.37				
	TRT	26 / 51	6.8	0.55	(0.29 – 1.02)	0.057	-
Mutant Age(<66%, 59)	CTRL	19 / 25	3.14				
	TRT	18 / 36	5.72	0.4	(0.21 – 0.76)	0.0052	-
Wild Type Age(<66%, 58)	CTRL	31 / 44	4.37				
	TRT	52 / 105	6.8	0.43	(0.27 – 0.68)	0.00028	
							0 0.5 1 1.5 2 2.5 TRT better [HR] CTRL better

2-arm, compare subgroups defined by biomarker, multiple cutoffs for continuous biomarker, calculate "< cutoff"

Across arm, Compare KRAS.mutant subgroup PFS Unadjusted, unstratified analysis

Subgroup	Group	Event/N	MST	HR	(CI)	raw P	
Mutant Sex(F)	CTRL	13 / 15	3.17				
	TRT	22 / 35	5.22	0.53	(0.27 – 1.05)	0.069	_
Wild Type Sex(F)	CTRL	20 / 32	4.47				
	TRT	42 / 76	6.31	0.54	(0.31 – 0.94)	0.03	-
Mutant Sex(M)	CTRL	13 / 19	3.22				
	TRT	9 / 26	8.31	0.35	(0.15 – 0.83)	0.017	-
Wild Type Sex(M)	CTRL	27 / 37	3.02				
	TRT	45 / 86	6.67	0.47	(0.29 – 0.76)	0.0023	-
Mutant Age(>=33%, 49)	CTRL	19 / 22	3.06				
	TRT	23 / 42	5.59	0.53	(0.29 – 0.98)	0.043	-
Wild Type Age(>=33%, 48)	CTRL	30 / 44	3.94				
	TRT	61 / 111	6.31	0.49	(0.31 – 0.76)	0.0017	-
Mutant Age(>=66%, 59)	CTRL	7/9	5.78				
	TRT	13 / 25	6.18	0.87	(0.32 – 2.38)	0.79	
Wild Type Age(>=66%, 58)	CTRL	16 / 25	3.38				
	TRT	35 / 57	5.49	0.63	(0.35 – 1.16)	0.14	-
Mutant Age(<33%, 49)	CTRL	7 / 12	3.56				
	TRT	8 / 19	8.31	0.4	(0.15 – 1.13)	0.083	-
Wild Type Age(<33%, 48)	CTRL	17 / 25	4.37				
	TRT	26 / 51	6.8	0.55	(0.29 – 1.02)	0.057	-
Mutant Age(<66%, 59)	CTRL	19 / 25	3.14				
	TRT	18 / 36	5.72	0.4	(0.21 – 0.76)	0.0052	-
Wild Type Age(<66%, 58)	CTRL	31 / 44	4.37				
	TRT	52 / 105	6.8	0.43	(0.27 – 0.68)	0.00028	
							0 0.5 1 1.5 2 2.5 TRT better [HR] CTRL better

2-arm, compare subgroups defined by biomarker, multiple cutoffs for continuous biomarker, calculate within bin statistics

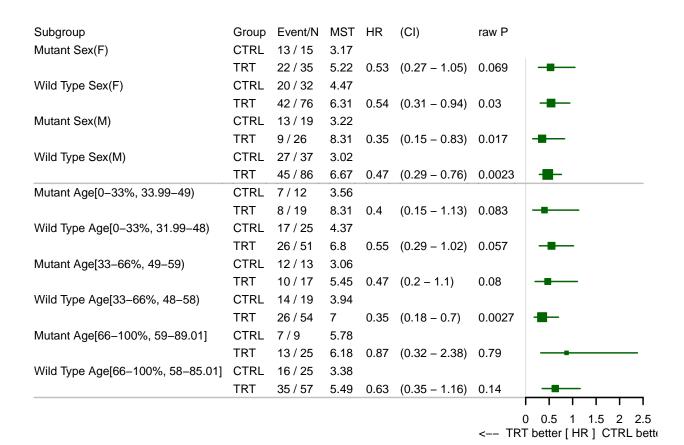
```
PlotTabForestMulti(data=input,

outcome.class="survival",
outcome.var=c("PFS","PFS.event"),
trt="Arm", percentile.cutoff=c(.33,.66),within.bin=TRUE,
var=c("Sex","Age"),
bep="BEP",bep.indicator=1, compare.bep.itt=FALSE,
compare.subgroup=TRUE, subgroup="KRAS.mutant"
)
```

```
## within.bin is TRUE, greater and less will be ignored
## within.bin is TRUE, greater and less will be ignored
## within.bin is TRUE, greater and less will be ignored
## within.bin is TRUE, greater and less will be ignored
```

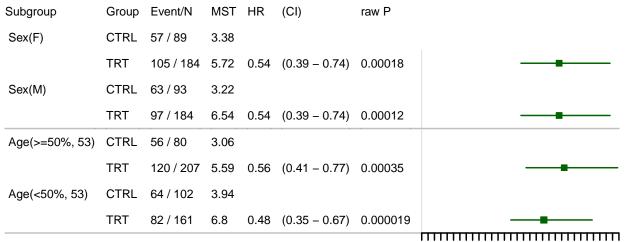
Across arm, Compare KRAS.mutant subgroup PFS

Unadjusted, unstratified analysis



Basic forest plot without comparison

Across arm PFS Unadjusted, unstratified analysis



00.075 0.2 0.3 0.4 0.5 0.6 0.7 <-- TRT better [HR] CTRL better --->

Response outcome

Covariate adjustment and stratification are not supported for binary outcome ## Covariate adjustment and stratification are not supported for binary outcome

Across arm Response Unadjusted, unstratified analysis

Subgroup	Group	nRsp/N	Rsp Rate	deltaRR	(CI)	raw P	
Sex(F)	CTRL	9 / 89	0.1				
	TRT	45 / 184	0.24	0.14	(0.05 – 0.24)	0.0086	
Sex(M)	CTRL	5/93	0.05				
	TRT	51 / 184	0.28	0.22	(0.14 – 0.31)	0.000025	-
Age(>=50%, 53)	CTRL	6 / 80	0.08				
	TRT	50 / 207	0.24	0.17	(0.08 – 0.26)	0.0025	
Age(<50%, 53)	CTRL	8 / 102	0.08				
	TRT	46 / 161	0.29	0.21	(0.11 – 0.3)	0.000097	

0.044 0.088 0.177 0.354 0.707 <-- CTRL better [deltaRR] TRT better

```
PlotTabForestMulti(data=input, outcome.class="binary", outcome.var=c("Response"), rsp.cat = TRUE, rsp.response = c("CR","PR"), rsp.nonresponse = c("SD", "PD","NON CR/PD","NE",NA), trt="Arm", var=c("Sex","Age"), compare.bep.itt=FALSE, compare.subgroup=FALSE,itt.name="", tabforest=T)
```

Covariate adjustment and stratification are not supported for binary outcome ## Covariate adjustment and stratification are not supported for binary outcome

Warning in log(clip): NaNs produced

Across arm Response

Subgroup	Group	nRsp/N	Rsp Rate	deltaRR	CI	raw P	Fores	t plot
							TRT better	CTRL better
Sex(F)	CTRL	9 / 89	0.1					
	TRT	45 / 184	0.24	0.14	0.05 – 0.24	0.0086 —		•
Sex(M)	CTRL	5 / 93	0.05					
	TRT	51 / 184	0.28	0.22	0.14 – 0.31	0.000025		
Age(>=50%, 53)	CTRL	6 / 80	0.08					
	TRT	50 / 207	0.24	0.17	0.08 - 0.26	0.0025		•
Age(<50%, 53)	CTRL	8 / 102	0.08					
	TRT	46 / 161	0.29	0.21	0.11 – 0.3	0.000097		•
		Unadjusted,	unstratified	d analysis			0.1	0.2 0

Continuous endpoint

Stratification is not supported for continuous outcome
Stratification is not supported for continuous outcome

Across arm Lab_ontrt Unadjusted, unstratified analysis

Subgroup	Group	Mean	delta	(CI)	raw P										
Sex(F)	CTRL	18.86													
	TRT	22.11	3.25	(1.38 – 5.11)	0.00073				_			-			
Sex(M)	CTRL	19.57													
	TRT	22.24	2.67	(0.82 – 4.51)	0.0048						_				
Age(>=50%, 53)	CTRL	19.1													
	TRT	22.05	2.95	(1.07 – 4.83)	0.0022			-			-	<u> </u>			-
Age(<50%, 53)	CTRL	19.32													
	TRT	22.33	3.01	(1.14 – 4.87)	0.0017			-			_	_			_
													1		\neg
						0	0.5 <							4.5 >	

Stratification is not supported for continuous outcome
Stratification is not supported for continuous outcome

Across arm Lab ontrt

Subgroup	Group	Mean	delta	CI	raw P	Forest plot
						TRT befterRL bette
Sex(F)	CTRL	18.86				!
	TRT	22.11	3.25	1.38 – 5.11	0.00073	•
Sex(M)	CTRL	19.57				
	TRT	22.24	2.67	0.82 – 4.51	0.0048	•
Age(>=50%, 53)	CTRL	19.1				
	TRT	22.05	2.95	1.07 – 4.83	0.0022	•
Age(<50%, 53)	CTRL	19.32				
	TRT	22.33	3.01	1.14 – 4.87	0.0017	•
	Unadjusted, unstr	ratified analysis				-4 0 2 4

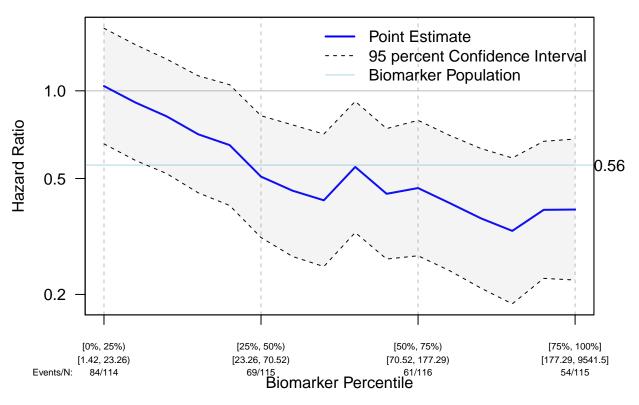
PlotSTEPP(): STEPP (Subpopulation Treatment Effect Pattern Plot) from the given point estimates and confidence intervals at desired percentiles.

Survival outcome

```
PlotSTEPP(data = input,
          outcome.var = c("PFS", "PFS.event"),
          outcome.class = "survival",
          trt = "Arm",
          var = "KRAS.exprs",
          placebo.code = "CTRL",
          active.code = "TRT",
          csv.name = NULL,
         pdf.name = NULL
```

some NA in var column, will ignore NA entries





##		Window Center Ha	zard Ratio	CI Lower	CI Upper	BM Lower	BM Upper
##	[1,]	0.125	1.0382905	0.6576013	1.6393629	1.42	23.26
##	[2,]	0.175	0.9116623	0.5769829	1.4404727	5.98	32.00
##	[3,]	0.225	0.8168277	0.5196594	1.2839325	9.51	42.81
##	[4,]	0.275	0.7091655	0.4465512	1.1262218	14.03	48.84
##	[5,]	0.325	0.6512376	0.4040444	1.0496628	19.70	59.30
##	[6,]	0.375	0.5074886	0.3136041	0.8212413	23.26	70.52
##	[7,]	0.425	0.4542622	0.2700666	0.7640860	32.00	77.71
##	[8,]	0.475	0.4208886	0.2493019	0.7105732	42.81	95.01
##	[9,]	0.525	0.5477689	0.3262293	0.9197544	48.84	121.94
##	[10,]	0.575	0.4430307	0.2645633	0.7418874	59.30	151.17
	[11,]	0.625					
##	[12,]	0.675	0.4121338	0.2414306	0.7035327	77.71	213.78
##	[13,]	0.725	0.3650580	0.2102587	0.6338257	95.01	259.57
##	[14,]	0.775	0.3304610	0.1856466	0.5882385	121.94	317.37
##	[15,]	0.825	0.3903051	0.2270411	0.6709713	151.17	467.88
##	[16,]	0.875	0.3912302	0.2241152	0.6829571	177.29	9541.50
##		BM Center Window	Left Windo	ow Right	N Events		
##	[1,]	11.010	0.00	0.25 1	14 84		
##	-	16.450					
##		21.860			15 85		
##	[4,]	27.860	0.15	0.40 1	15 78		
##	[5,]	36.250	0.20	0.45 1	15 73		
##	[6,]	45.250	0.25	0.50 1	15 69		
##	[7,]	53.265	0.30	0.55 1	14 59		
##		64.450	0.35	0.60 1	15 59		
##	[9,]	73.010	0.40	0.65 1	15 63		

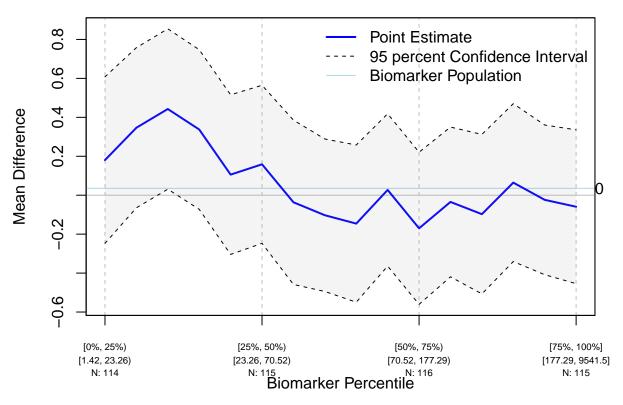
```
## [10,]
                           0.45
                                         0.70 115
            88.030
                                                       62
## [11,]
           101.480
                           0.50
                                         0.75 116
                                                       61
                           0.55
                                         0.80 116
## [12,]
           133.900
                                                       61
## [13,]
                           0.60
                                                       55
           165.420
                                         0.85 115
## [14,]
           195.360
                           0.65
                                         0.90 115
                                                       51
## [15,]
           238.860
                           0.70
                                         0.95 115
                                                       56
## [16,]
           292.040
                           0.75
                                         1.00 115
```

Continuous outcome

##

 $\mbox{\tt \#\#}$ some NA in var column, will ignore NA entries

STEPP: Subgroup Treatment Effect Pattern Plot



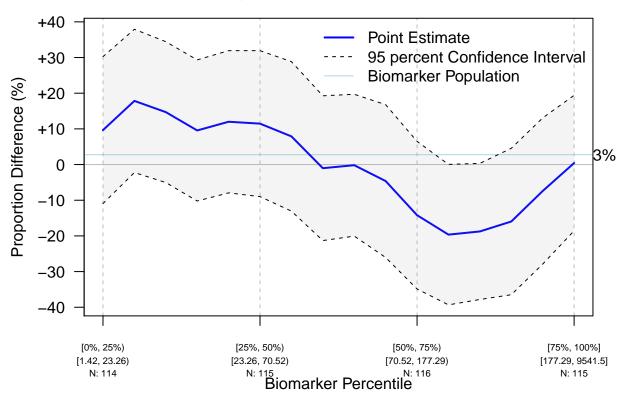
Window Center Mean Difference CI Lower CI Upper BM Lower

```
[1,]
##
                 0.125
                             0.18035575 -0.24729997 0.6080115
                                                                   1.42
##
    [2,]
                 0.175
                             0.34651479 -0.06475305 0.7577826
                                                                   5.98
                             0.44278821 0.03092580 0.8546506
##
   [3,]
                 0.225
                                                                   9.51
   [4,]
                             0.33749063 -0.07236992 0.7473512
##
                 0.275
                                                                  14.03
##
   [5,]
                 0.325
                             0.10572728 -0.30412158 0.5155761
                                                                  19.70
##
   [6,]
                             0.15866042 -0.24724256 0.5645634
                                                                  23.26
                 0.375
##
   [7,]
                            -0.03630432 -0.45831952 0.3857109
                                                                  32.00
                 0.425
## [8,]
                            -0.10286329 -0.49436652 0.2886399
                 0.475
                                                                  42.81
## [9,]
                 0.525
                            -0.14583073 -0.54953031 0.2578689
                                                                  48.84
## [10,]
                             0.02704796 -0.36419706 0.4182930
                 0.575
                                                                  59.30
## [11,]
                 0.625
                            -0.16994763 -0.56071364 0.2208184
                                                                  70.52
## [12,]
                 0.675
                            -0.03456171 -0.41907553 0.3499521
                                                                  77.71
## [13,]
                 0.725
                            -0.09734050 -0.50684711 0.3121661
                                                                  95.01
                             0.06465414 -0.34072771 0.4700360
## [14,]
                 0.775
                                                                 121.94
## [15,]
                 0.825
                            -0.02383926 -0.40821143 0.3605329
                                                                 151.17
## [16,]
                 0.875
                            -0.05926090 -0.45420790 0.3356861
                                                                 177.29
##
         BM Upper BM Center Window Left Window Right
                                    0.00
##
    [1,]
            23.26
                      11.010
                                                  0.25 114
##
   [2,]
            32.00
                     16.450
                                    0.05
                                                  0.30 115
##
   [3,]
            42.81
                     21.860
                                    0.10
                                                  0.35 115
##
  [4,]
            48.84
                     27.860
                                    0.15
                                                  0.40 115
##
  [5,]
            59.30
                     36.250
                                    0.20
                                                  0.45 115
  [6,]
##
            70.52
                     45.250
                                    0.25
                                                  0.50 115
##
   [7,]
            77.71
                     53.265
                                    0.30
                                                  0.55 114
                                                  0.60 115
##
  [8,]
            95.01
                     64.450
                                    0.35
  [9,]
           121.94
                     73.010
                                    0.40
                                                  0.65 115
## [10,]
           151.17
                     88.030
                                    0.45
                                                  0.70 115
## [11,]
           177.29
                    101.480
                                    0.50
                                                  0.75 116
## [12,]
           213.78
                    133.900
                                    0.55
                                                  0.80 116
## [13,]
           259.57
                    165.420
                                    0.60
                                                  0.85 115
## [14,]
           317.37
                    195.360
                                    0.65
                                                  0.90 115
## [15,]
           467.88
                    238.860
                                    0.70
                                                  0.95 115
## [16,]
          9541.50
                    292.040
                                    0.75
                                                  1.00 115
```

Binary outcome variable

some NA in var column, will ignore NA entries

STEPP: Subgroup Treatment Effect Pattern Plot



##		Window Center	Propor	tion Dif	ference	CI Lower	(CI Upper
##	[1,]	0.125	·	0.09	6558637	-0.10936788	0.302	24851571
##	[2,]	0.175)	0.17	8408350	-0.02235039	0.379	91670900
##	[3,]	0.225)	0.14	7000659	-0.05041839	0.344	14197101
##	[4,]	0.275)	0.09	5583388	-0.10218602	0.293	3527961
##	[5,]	0.325)	0.11	9973632	-0.07934753	0.319	92947989
##	[6,]	0.375	ò	0.11	4700066	-0.08986157	0.319	92616985
##	[7,]	0.425	ò	0.07	8947368	-0.13057600	0.288	34707407
##	[8,]	0.475)	-0.01	0179010	-0.21308461	0.192	27265895
##	[9,]	0.525)	-0.00	1808318	-0.20059338	0.196	39767445
##	[10,]	0.575	;	-0.04	6292948	-0.26043294	0.167	78470400
##	[11,]	0.625	;	-0.14	1906874	-0.34878874	0.064	19749952
##	[12,]	0.675)	-0.19	6428571	-0.39328032	0.000)4231801
##	[13,]	0.725	;	-0.18	7500000	-0.37820558	0.003	32055783
##	[14,]	0.775	;	-0.15	9638554	-0.36486679	0.045	55896813
##	[15,]	0.825	;	-0.07	4191280	-0.27905945	0.130	6768944
##	[16,]	0.875	j	0.00	4219409	-0.18560507	0.194	10438921
##		BM Lower BM U	Jpper BM	Center	Window 1	Left Window H	Right	N
##	[1,]	1.42	23.26	11.010	(0.00	0.25	114
##	[2,]	5.98	32.00	16.450	(0.05	0.30	115
##	[3,]	9.51 4	2.81	21.860	(0.10	0.35	115
##	[4,]	14.03	8.84	27.860	(0.15	0.40	115
##	[5,]	19.70	9.30	36.250	(0.20	0.45	115
##	[6,]	23.26 7	0.52	45.250	(0.25	0.50	115
##	[7,]	32.00 7	7.71	53.265	(0.30	0.55	114
##	[8,]	42.81	5.01	64.450	(0.35	0.60	115
##	[9,]	48.84 12	21.94	73.010	(0.40	0.65	115

```
## [10,]
          59.30 151.17
                                        0.45
                                                    0.70 115
                           88.030
## [11,]
          70.52 177.29
                          101.480
                                        0.50
                                                    0.75 116
## [12,]
          77.71 213.78 133.900
                                        0.55
                                                    0.80 116
## [13,]
          95.01
                  259.57 165.420
                                        0.60
                                                    0.85 115
         121.94 317.37
## [14,]
                         195.360
                                        0.65
                                                    0.90 115
## [15,]
         151.17 467.88
                          238.860
                                        0.70
                                                    0.95 115
## [16,]
          177.29 9541.50
                          292.040
                                        0.75
                                                    1.00 115
```

CoxTab(): fit cox proportional model for multiple covariates (additive model or separate models)

single covariate

```
CoxTab(data=sample.data, tte="OS", cens="OS.event",bep='BEP', var='Sex')

## HR CI.low CI.high p-value n.trt n.ref

## Sex (M/F) "0.85" "0.42" "1.72" "0.65" "128" "129"
```

multiple covariates, ITT

Additive model will be fitted.

	HR	CI.low	CI.high	p-value	n.trt	n.ref
Sex (M/F)	0.72	0.48	1.08	0.11	277	273
Country (USA/Other)	0.65	0.36	1.2	0.17	127	198
Country (Western Europe/Other)	0.77	0.5	1.2	0.24	225	198
Age	1.01	0.99	1.03	0.43		

Simplify: automatically learn var.class from column class:

```
kable(
CoxTab(data=sample.data,tte="OS", cens="OS.event", var=c('Sex',"Country","Age"))
)
```

	HR	CI.low	CI.high	p-value	n.trt	n.ref
Sex (M/F)	0.72	0.48	1.08	0.11	277	273
Country (USA/Other)	0.65	0.36	1.2	0.17	127	198
Country (Western Europe/Other)	0.77	0.5	1.2	0.24	225	198
Age	1.01	0.99	1.03	0.43		

BEP

	HR	CI.low	CI.high	p-value	n.trt	n.ref
Sex (M/F)	0.85	0.42	1.73	0.65	128	129
Country (USA/Other)	1.17	0.4	3.38	0.77	76	57
Country (Western Europe/Other)	1.11	0.44	2.83	0.83	124	57
Age	1.01	0.98	1.04	0.48		

Reorder Sex: M as reference

HR	CI.low	CI.high	p-value	n.trt	n.ref
1.12	0.68	1.85	0.65	129	128
1.17	0.4	3.38	0.77	76	57
1.11	0.44	2.83	0.83	124	57
1.01	0.98	1.04	0.48		
	1.12 1.17 1.11	1.12 0.68 1.17 0.4 1.11 0.44	1.12 0.68 1.85 1.17 0.4 3.38 1.11 0.44 2.83	1.12 0.68 1.85 0.65 1.17 0.4 3.38 0.77 1.11 0.44 2.83 0.83	1.17 0.4 3.38 0.77 76 1.11 0.44 2.83 0.83 124

Fit separate models for each variable instead of fitting an additive model

	HR	CI.low	CI.high	p-value	n.trt	n.ref
Sex (M/F)	0.71	0.48	1.07	0.099	277	273
Country (USA/Other)	0.67	0.37	1.22	0.19	127	198
Country (Western Europe/Other)	0.77	0.5	1.2	0.25	225	198
Age	1.01	0.99	1.02	0.54		

SummaryTwoGroups()

Contunuous outcome

Create summary statistics

```
SummaryTwoGroups(outcome.var = input$OS, treatment.var = input$Arm,
            placebo.code = "CTRL", active.code = "TRT",
            outcome.class = "continuous")
##
   Effect.Size
                       Lower
                                                     P Mean.Placebo
                                    Upper
##
    0.79113129
                  0.19464513
                               1.38761744
                                            0.00942898
                                                        5.77854999
## Mean.Active
    6.56968128
```

Add a covariate variable

Add return.fit = TRUE to return a table of summary statistics

```
## [[1]]
## Effect.Size
                                                     P Mean.Placebo
                       Lower
                                    Upper
## 0.795751256 0.199865806 1.391636707 0.008954882 5.563721382
## Mean.Active
## 6.359472638
##
## [[2]]
##
## Call:
## lm(formula = outcome.var[subgroup.var] ~ covariate.var[subgroup.var] +
      treatment.var[subgroup.var])
##
##
## Coefficients:
##
                      (Intercept)
                                     covariate.var[subgroup.var]M
                                                           0.4204
##
                           5.5637
## treatment.var[subgroup.var]TRT
                           0.7958
##
```

Binary outcome

Create summary statistics

```
SummaryTwoGroups(outcome.var = input$0S.event, treatment.var = input$Arm,
           placebo.code = "CTRL", active.code = "TRT",
           outcome.class = "binary")
## Effect.Size
                      Lower
                                   Upper
                                                    P Rsp.Placebo
  -0.04846512 -0.12251455
                              0.02558430
                                           0.19901328
                                                        0.20879121
##
    Rsp.Active
                  N.Placebo
                                N.Active nRsp.Placebo nRsp.Active
    0.16032609 182.00000000 368.00000000 38.00000000 59.00000000
```

Survival variable

Create summary statistics

```
SummaryTwoGroups(outcome.var = input[, c("OS", "OS.event")],
            treatment.var = input$Arm, placebo.code = "CTRL",
            active.code = "TRT", outcome.class = "survival")
## CTRL.events
                    CTRL.n
                              CTRL.MST TRT.events
                                                         TRT.n
                                                                   TRT.MST
## 38.0000000 182.0000000 14.8829569 59.0000000 368.0000000
                                                                        NA
## Effect.Size
                     Lower
                                 Upper
                 0.4432032
     0.6667451
                             1.0030365
                                         0.0517253
```

Add a covariate variable

```
SummaryTwoGroups(outcome.var = input[, c("OS", "OS.event")],
            treatment.var = input$Arm, placebo.code = "CTRL",
            active.code = "TRT", outcome.class = "survival",
            covariate.var = input$Sex)
                                 CTRL.MST
   CTRL.events
                      CTRL.n
##
                                            TRT.events
                                                              TRT.n
   38.00000000 182.00000000 14.88295688
                                           59.00000000 368.00000000
##
        TRT.MST Effect.Size
                                    Lower
                                                 Upper
```

0.96401541

0.03277593

0.42390908

Add a stratification variable

NA

0.63926120

##

```
## CTRL.events
                    CTRL.n
                               CTRL.MST
                                         TRT.events
                                                           TRT.n
##
   38.00000000 182.00000000 14.88295688 59.00000000 368.00000000
       TRT.MST Effect.Size
##
                                  Lower
                                              Upper
##
                0.60116855 0.37830923
                                         0.95531273
                                                      0.03128551
            NA
```

LogRankTab(): log rank test for subgroup analysis

```
kable(
  LogRankTab(data=input,tte="PFS",cens="PFS.event",var="Arm")
)
```

	CTRL	TRT
	N=182	N = 368
Patients with event	120~(65.9%)	202 (54.9%)
Patients without event	62 (34.1%)	166 (45.1%)
Time to event (month)		
Median (KM)	3.25	5.82
95% CI Median	(2.83;4.14)	(5.49;6.8)
25% and $75%$ -ile	1.61;6.47	2.89;11.73
Range (inc. cens.)	0.03 to 12.32	0.03 to 13.8
p-value (Log-Rank Test)		0
Hazard Ratio		0.54
95% CI		(0.43;0.67)

BoxPlot(): advanced box plot function

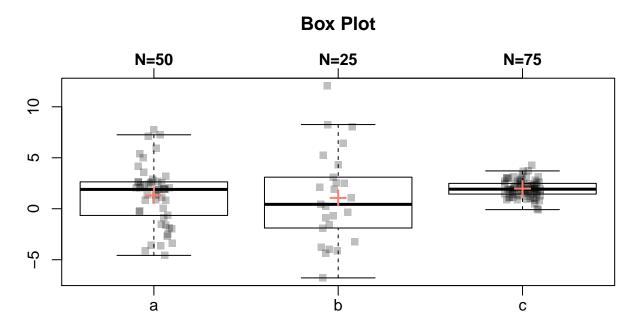
Generate example dataset

```
example <- data.frame(y=c(rnorm(30)+10, rnorm(4)+20, rnorm(15)+15, NA),
                          time=c(rep("t2", 30), rep("t4",4), rep("t1", 15), "t3"),
                          grp=sample(1:3, 50, TRUE), sex=sample(1:2, 50, TRUE))
head(example)
##
            y time grp sex
## 1 8.849692 t2
## 2 9.319510
              t2
                        1
## 3 9.696244
              t2 2
## 4 9.894096
              t2 2
## 5 10.492300
               t2
                   1
              t2 3
## 6 10.235155
str(example)
                  50 obs. of 4 variables:
## 'data.frame':
## $ y : num 8.85 9.32 9.7 9.89 10.49 ...
## $ time: Factor w/ 4 levels "t1","t2","t3",...: 2 2 2 2 2 2 2 2 2 2 ...
```

```
## $ grp : int 2 3 2 2 1 3 2 2 3 2 ...
## $ sex : int 1 1 2 2 2 1 2 2 2 1 ...
```

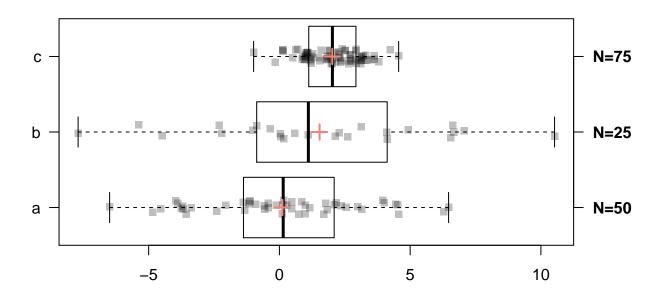
Specify data as named list

```
BoxPlot(list(a=rnorm(50,,3), b=rnorm(25,1,4), c=rnorm(75,2,1)))
```



Same plot, now horizontally plotted

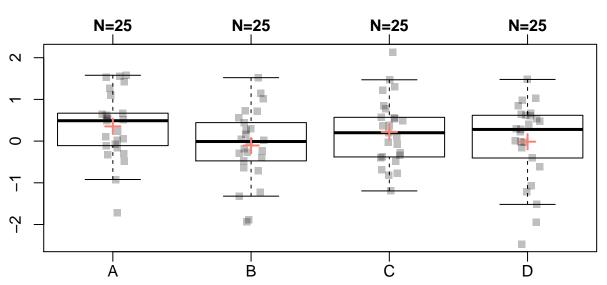
Box Plot



Specify data as numeric matrix

```
BoxPlot(matrix(rnorm(100), ncol=4, dimnames=list(NULL, LETTERS[1:4])) )
```

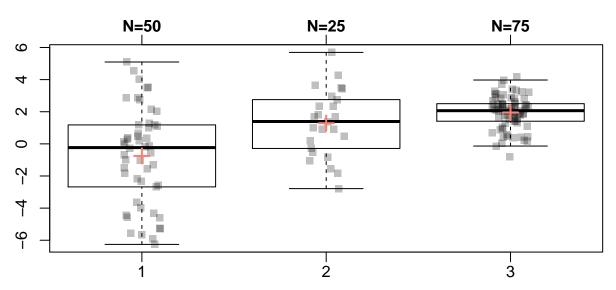




Specify data as numeric (unnamed) vectors

```
BoxPlot(rnorm(50,,3), rnorm(25,1,2), rnorm(75,2,1))
```

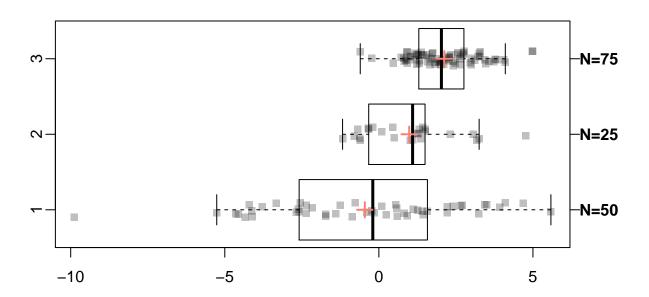
Box Plot



... horizontally plotted (no axis-label rotation done here)

```
BoxPlot(rnorm(50,,3), rnorm(25,1,2), rnorm(75,2,1), horizontal=TRUE)
```

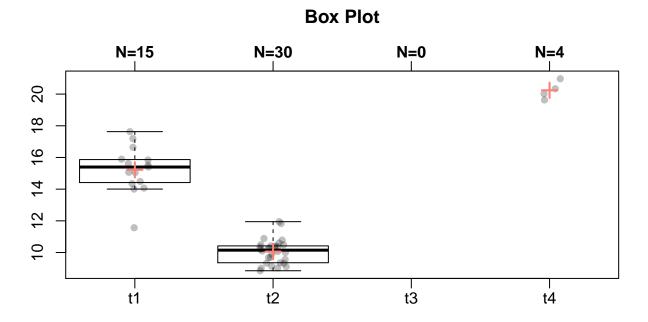
Box Plot



Plot values 'y' according to time 'time' (factor levels are automatically ordered as e.g. function sort does)

```
BoxPlot(example, y~time, sc.pch=16)
```

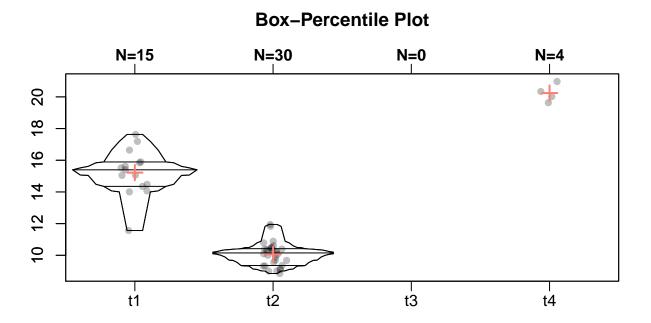
Number of samples removed due to missing Y: 1



Now as box-percentile plot

```
BoxPlot(example, y~time, sc.pch=16, box.type="bp")
```

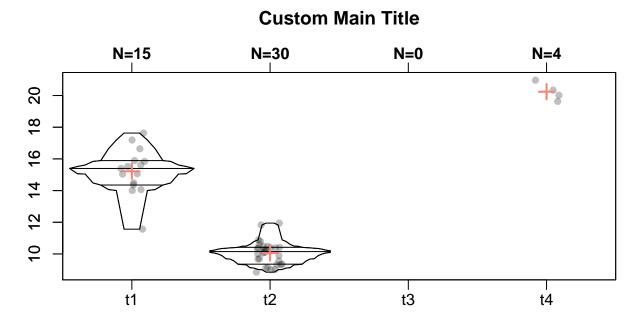
Number of samples removed due to missing $Y:\ 1$



With custom main title

```
BoxPlot(example, y~time, sc.pch=16, box.type="bp", Title=list(main="Custom Main Title"))
```

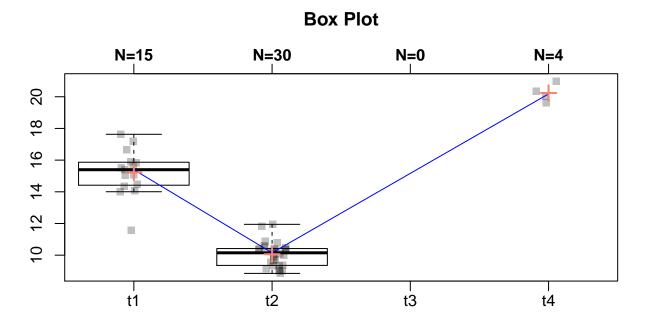
Number of samples removed due to missing Y: 1



The same plot with trend line (connects either means or medians) and Y-axis label

```
BoxPlot(example, y~time, trend="median", ylab="Y-Axis Label")
```

Number of samples removed due to missing Y: 1



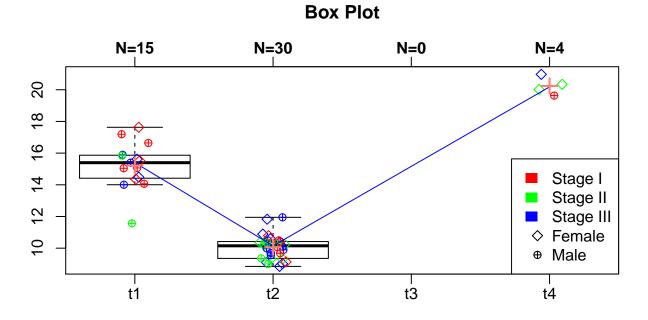
Use an addition grouping variable to color points in the stripchart

Number of samples removed due to missing Y: 1

N=15 N=30 N=0 N=4 07 81 91 17 12 13 14

Use yet another grouping factor for plotting symbols in the stripchart

Number of samples removed due to missing Y: 1

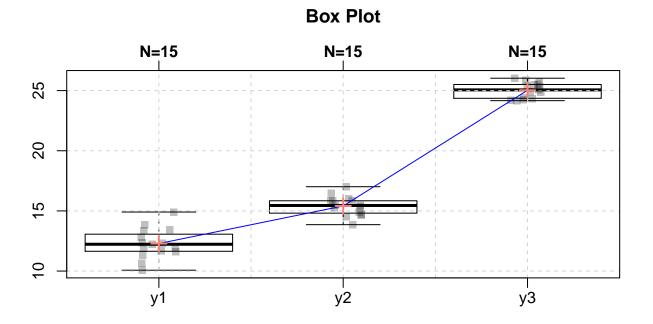


Generate new dataset with different stucture

```
example2 <- data.frame(y1=12+rnorm(15), y2=15+rnorm(15), y3=25+rnorm(15))
```

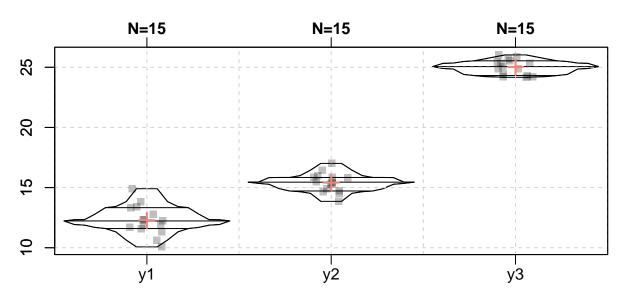
Boxplot with trend lines (mean) and grid added to the plot

```
BoxPlot(example2, var=c("y1", "y2", "y3"), Grid=TRUE, trend="mean")
```



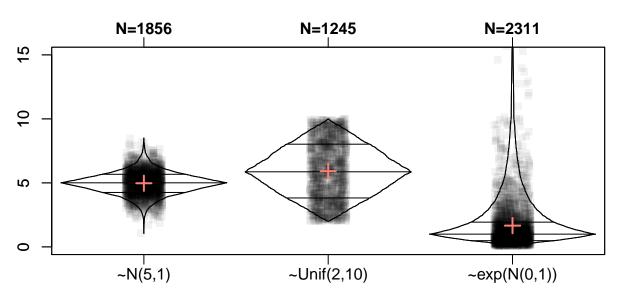
```
BoxPlot(example2, var=c("y1", "y2", "y3"), box.type="bp", Grid=TRUE)
```

Box-Percentile Plot



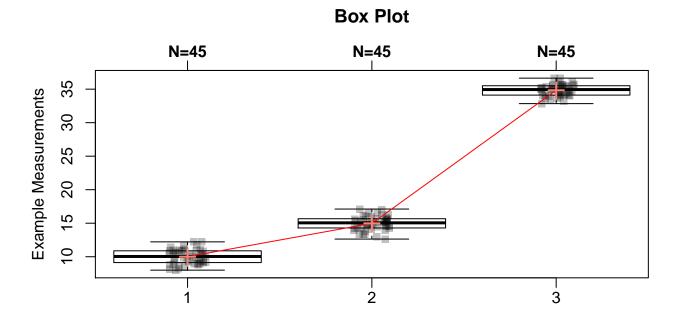
Use yet another way to specify the data

Box-Percentile Plot



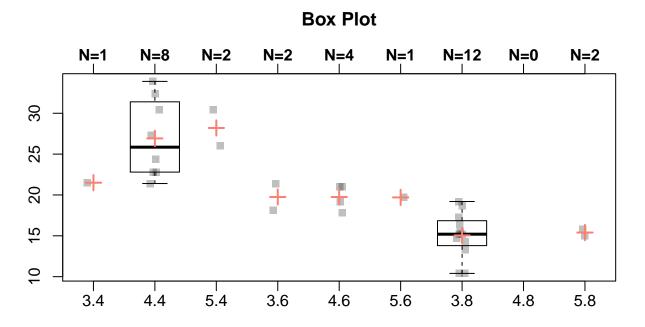
Specifying data as numeric matrix and using a trend-line connecting the means

```
mat <- matrix(c(rep(10,45), rep(15,45), rep(35,45))+rnorm(135), ncol=3)
BoxPlot(mat, trend="mean", trend.col="red", Ylabel=list(text="Example Measurements"))</pre>
```



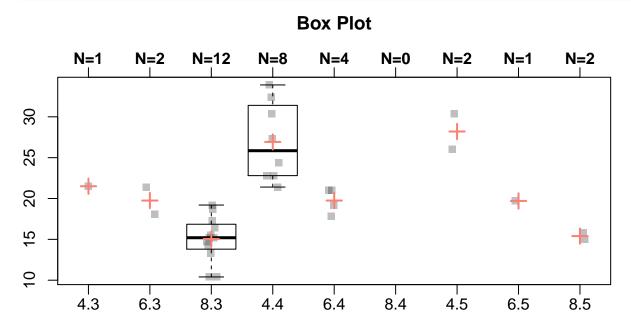
Multiple grouping factors can be specified via the formula interface which is exemplified using the mtcars dataset, of interest is miles per gallon (mgp) depending on number of gears and on the number of cylinders

```
data(mtcars)
BoxPlot(mtcars, mpg~gear:cyl)
```



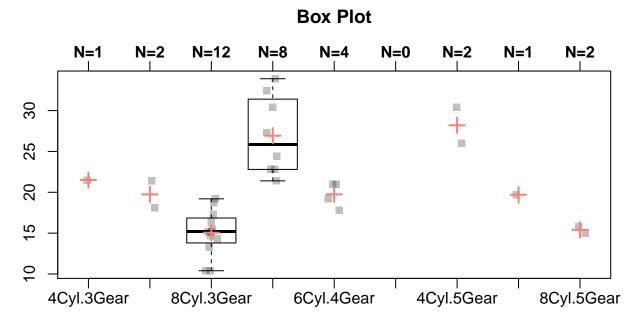
Now 'cyl' is explicitly nested within 'gear' which changes the ordering of combined grouping factors (which is identical to using formula 'mpg~cyl:gear').

BoxPlot(mtcars, mpg~cyl %in% gear)



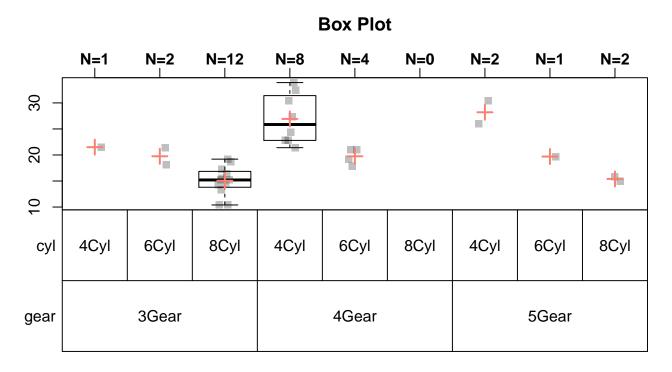
More meaningful group-labels are best specified using custom factor-level names (increase width of the plot window)

```
dat <- mtcars
dat$cyl <- factor(dat$cyl, levels=c(4,6,8), labels=c("4Cyl", "6Cyl", "8Cyl"))
dat$gear <- factor(dat$gear, levels=c(3,4,5), labels=c("3Gear", "4Gear", "5Gear"))
BoxPlot(dat, mpg~cyl %in% gear)</pre>
```



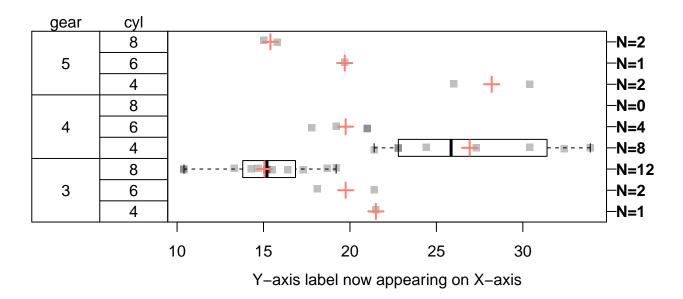
One can use a table as Xaxis label representing the factor-level combination defining sub-classes

```
BoxPlot(dat, mpg~cyl:gear, XaxisTab=list(),mar=c(8,3,5,1))
```



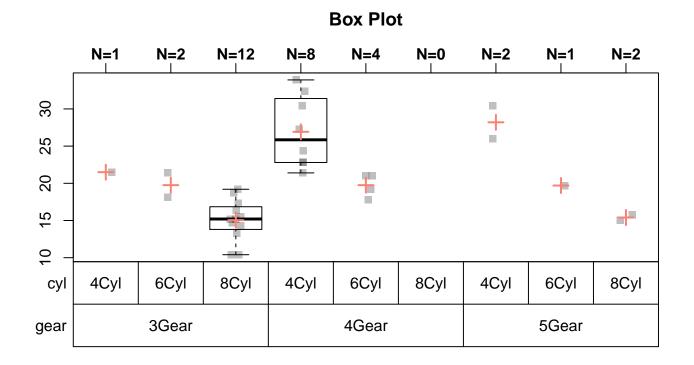
With the original factor levels and as horizontal plot

Box Plot

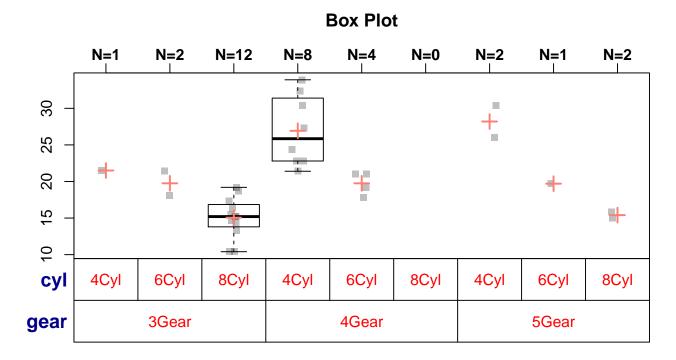


Using smaller bottom margin will result in smaller table height

BoxPlot(dat, mpg~cyl:gear, XaxisTab=list(font=2, col="darkblue", cex=1.25), mar=c(5,3,5,1))

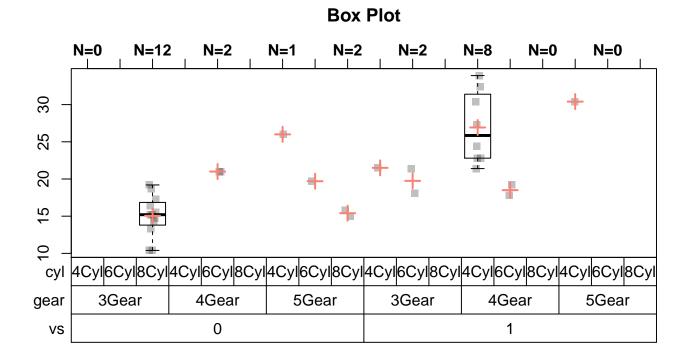


One can use different font-settings for rownames and cells of the table

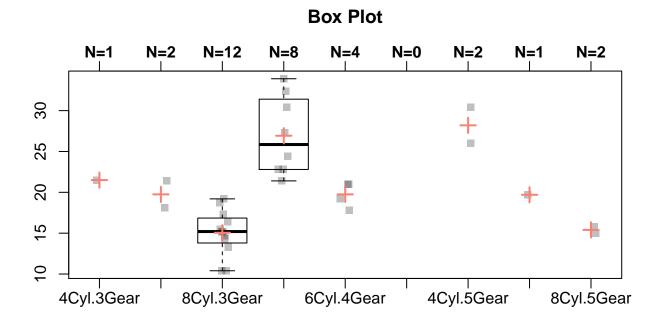


Use more crossed factors

```
BoxPlot(dat, mpg~cyl:gear:vs, XaxisTab=list(), mar=c(5,3,5,1))
```

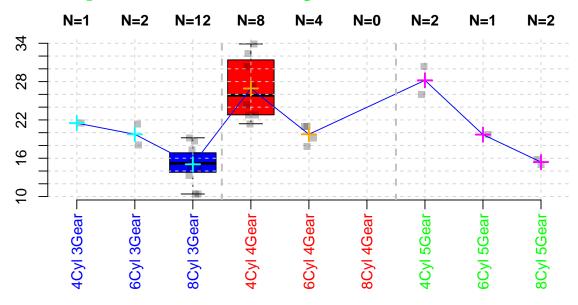


Alternatively one can use the 'Xaxis' argument, but the ordering of these labels is not checked which is not important for automatically generated group-labels as shown in the previous example



The same plot with some fancy options

Miles per Gallon by Number of Gea

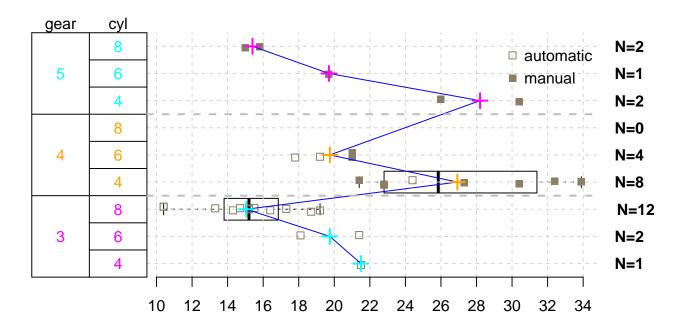


Horizontal fancy plot

```
BoxPlot(mtcars, mpg~cyl %in% gear, Title=list(main="Miles per Gallon by Number of Gears", col.main="#84
    vline=c(3.5, 6.5), vl.lty=2, vl.col="gray", vl.lwd=2,
        Xaxis2=list(tick=FALSE, las=2, hadj=-.25), Yaxis=list(at=seq(10,34,2)), Grid=list(x=1:9, y=seq(
        mean.col=c(rep("cyan", 3), rep("orange", 3), rep("magenta", 3)), Box=FALSE, trend="mean",
        mar=c(3, 7, 4, 4), horizontal=TRUE, sc.pch=c(0, 15)[dat$am+1], sc.col="wheat4",
        XaxisTab=list(Text=list(col=c(rep("cyan", 3), rep("orange", 3), rep("magenta", 3)))))

legend(x="topright", pch=c(0, 15), legend=c("automatic", "manual"), box.lty=0, col="wheat4")
```

Miles per Gallon by Number of Gears



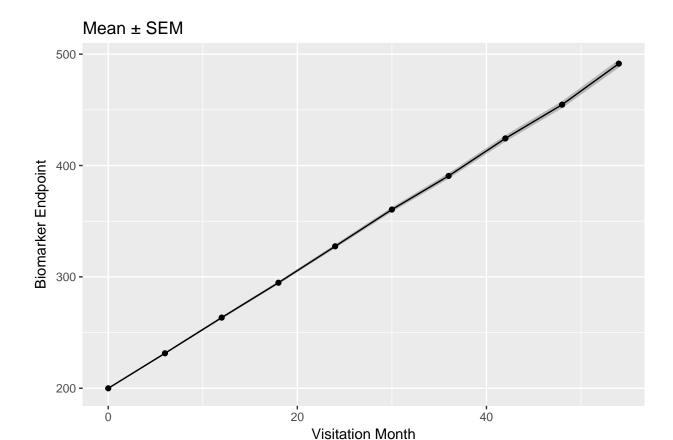
Longitudinal analysis

In the context of biomarker analysis, the PlotLong function can be used to plot the longitudinal measurement of a biomarker endpoint for one or more patient subpopulations. Here we'll use the packaged dataset bmkr (biomarker) which has columns for patient ID (pid), treatment (trt), gender (sex), visitation month (vm) and endpoint reading (ep)

Biomarker Endpoint Progression

Mean \pm SEM Timecourse

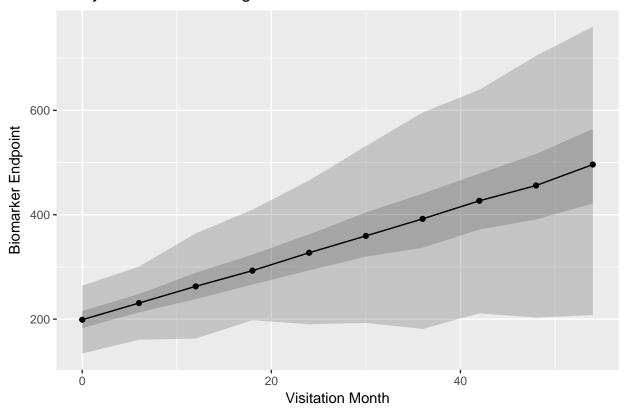
Here we plot the mean and standard error of the mean over time. We can see clearly that the mean biomarker endpoint increases throughout the study.



Tukey Hinges and Whiskers

However, we may be more interested in the population distribution progression where we'd want to plot the Tukey boxplot hinges and whiskers over time. From this plot, we can see that although there is a slow rise in population mean, the patient response also becomes more distributed.

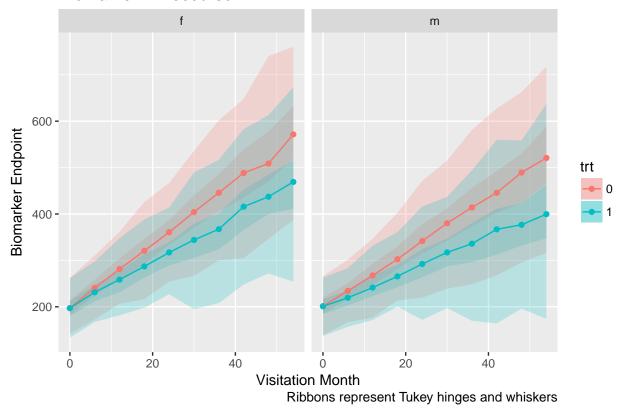
Tukey Whiskers and Hinges



Plotting Subpopulations

```
PlotLong(longbmkr, aes(x=vm, y=ep, group=trt, color=trt, fill=trt),
    fun.data = 'tukey', facet.fun = . ~ sex,
    xlab = 'Visitation Month',
    ylab = 'Biomarker Endpoint',
    labs.title = 'Biomarker Timecourse',
    labs.caption = 'Ribbons represent Tukey hinges and whiskers')
```

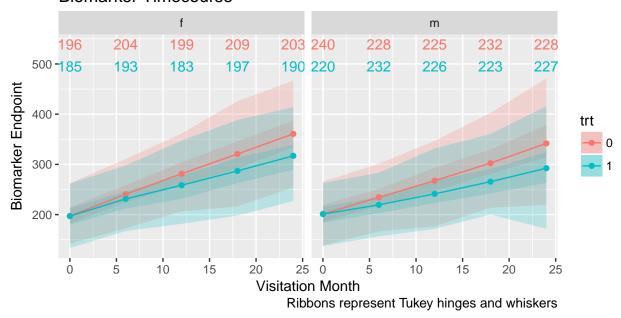
Biomarker Timecourse



Including sample counts

Sample counts as table above plot

Biomarker Timecourse



Plotting Deviations as Errorbars

Biomarker Timecourse

