

Sensitivity Analysis

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0. Setup

Reading packages

```
library(readxl)
library(ggplot2)
library(data.table)
library(Hmisc)
```

```
## Loading required package: lattice
```

```
## Loading required package: survival
```

```
## Loading required package: Formula
```

```
##
```

```
## Attaching package: 'Hmisc'
```

```
## The following objects are masked from 'package:base':
```

```
##
```

```
##      format.pval, units
```

```
library(dplyr)
```

```
##
```

```
## Attaching package: 'dplyr'
```

```
## The following objects are masked from 'package:Hmisc':
```

```
##
```

```
##      src, summarize
```

```
## The following objects are masked from 'package:data.table':
```

```
##
```

```
##      between, first, last
```

```
## The following objects are masked from 'package:stats':
```

```
##
```

```
##      filter, lag
```

```
## The following objects are masked from 'package:base':
```

```
##
```

```
##      intersect, setdiff, setequal, union
```

```
library(tidyr)
library(stringr)
library(binom)
library(gridExtra)
```

```
##
## Attaching package: 'gridExtra'

## The following object is masked from 'package:dplyr':
##
##      combine
```

```
library(grid)
```

Creating file paths

```
if(Sys.info()["user"]=="JVARGH7"){
  path_ic_documentation <- "C:/code/support/interstitial_cystitis/documentation"
  path_ic_data <- "C:/Cloud/OneDrive - Emory University/Papers/Interstitial Cystitis/data"
  path_ic_save <- "C:/Cloud/OneDrive - Emory University/Papers/Interstitial Cystitis/working"
}
```

1. Data Cleaning

Reading the data into R

```
ic_sensitivity <- readxl::read_xlsx(paste0(path_ic_data,"/De-identified covariates data_20190102.xlsx"))
```

```
colnames(ic_sensitivity) <- c("id","ic_list","cases",
                             "age_last_visit","gender","race","smoking",
                             "elmiron","hydroxyzine","tca","gabapentin","hydroxychloroquine",
                             "cyclobenzaprine","methenamine","phenazopyridine","oxybutynin")
ic_sensitivity <- ic_sensitivity %>% filter(!is.na(id))
```

```
ic_sensitivity <- ic_sensitivity %>% filter(!is.na(ic_list))
```

Labeling different columns

```
ic_sensitivity$cases <- as.factor(ic_sensitivity$cases)
levels(ic_sensitivity$cases) <- c("1 Definite","2 Possibly", "3 Not", "4 No images")
table(ic_sensitivity$cases,useNA = "always")
```

```
##
## 1 Definite 2 Possibly 3 Not 4 No images <NA>
##          3          4          32          126          0
```

```
ic_sensitivity$gender <- as.factor(ic_sensitivity$gender)
levels(ic_sensitivity$gender) <- c("1 Female", "2 Male")
table(ic_sensitivity$gender, useNA= "always")
```

```
##
## 1 Female    2 Male      <NA>
##      148      17        0
```

```
ic_sensitivity$race <- as.factor(ic_sensitivity$race)
levels(ic_sensitivity$race) <- c("1 White", "2 Black", "3 Other")
table(ic_sensitivity$race, useNA = "always")
```

```
##
## 1 White 2 Black 3 Other    <NA>
##      115      39      11      0
```

```
ic_sensitivity$smoking <- as.factor(ic_sensitivity$smoking)
levels(ic_sensitivity$smoking) <- c("1 Never", "2 Current", "3 Former")
table(ic_sensitivity$smoking, useNA = "always")
```

```
##
## 1 Never 2 Current 3 Former    <NA>
##      118      4      35      8
```

```
ic_sensitivity$elmiron <- with(ic_sensitivity, ifelse(!is.na(elmiron), 1, 0))
ic_sensitivity$hydroxyzine <- with(ic_sensitivity, ifelse(!is.na(hydroxyzine), 1, 0))
ic_sensitivity$tca <- with(ic_sensitivity, ifelse(!is.na(tca), 1, 0))
ic_sensitivity$gabapentin <- with(ic_sensitivity, ifelse(!is.na(gabapentin), 1, 0))
ic_sensitivity$hydroxychloroquine <- with(ic_sensitivity, ifelse(!is.na(hydroxychloroquine), 1, 0))
ic_sensitivity$cyclobenzaprine <- with(ic_sensitivity, ifelse(!is.na(cyclobenzaprine), 1, 0))
ic_sensitivity$methenamine <- with(ic_sensitivity, ifelse(!is.na(methenamine), 1, 0))
ic_sensitivity$phenazopyridine <- with(ic_sensitivity, ifelse(!is.na(phenazopyridine), 1, 0))
ic_sensitivity$oxybutynin <- with(ic_sensitivity, ifelse(!is.na(oxybutynin), 1, 0))

ic_sensitivity <- ic_sensitivity %>% mutate_at(c("elmiron", "hydroxyzine",
        "tca", "gabapentin", "hydroxychloroquine",
        "cyclobenzaprine", "methenamine",
        "phenazopyridine", "oxybutynin"),
        funs(factor(., labels=c("no", "yes"))))
```

Generating Summary Statistics: The variable ID has been ignored.

```
describe(ic_sensitivity %>% select(-id, -ic_list))
```

```
## ic_sensitivity %>% select(-id, -ic_list)
##
## 14 Variables      165 Observations
## -----
## cases
##      n missing distinct
##      165      0        4
##
## Value      1 Definite  2 Possibly      3 Not  4 No images
## Frequency           3        4        32       126
## Proportion      0.018      0.024      0.194      0.764
```

```

## -----
## age_last_visit
##      n  missing distinct      Info      Mean      Gmd      .05      .10
##    165      0      59    0.999    61.47    17.79    36.0    39.4
##      .25      .50      .75      .90      .95
##    50.0    64.0    73.0    80.0    85.6
##
## lowest : 24 25 28 29 31, highest: 86 87 88 89 90
## -----
## gender
##      n  missing distinct
##    165      0      2
##
## Value      1 Female      2 Male
## Frequency      148      17
## Proportion      0.897      0.103
## -----
## race
##      n  missing distinct
##    165      0      3
##
## Value      1 White 2 Black 3 Other
## Frequency      115      39      11
## Proportion      0.697      0.236      0.067
## -----
## smoking
##      n  missing distinct
##    157      8      3
##
## Value      1 Never 2 Current 3 Former
## Frequency      118      4      35
## Proportion      0.752      0.025      0.223
## -----
## elmiron
##      n  missing distinct
##    165      0      2
##
## Value      no  yes
## Frequency      125      40
## Proportion 0.758 0.242
## -----
## hydroxyzine
##      n  missing distinct
##    165      0      2
##
## Value      no  yes
## Frequency      126      39
## Proportion 0.764 0.236
## -----
## tca
##      n  missing distinct
##    165      0      2
##
## Value      no  yes

```

```

## Frequency    117    48
## Proportion 0.709 0.291
## -----
## gabapentin
##      n missing distinct
##    165      0        2
##
## Value      no  yes
## Frequency   100   65
## Proportion 0.606 0.394
## -----
## hydroxychloroquine
##      n missing distinct
##    165      0        2
##
## Value      no  yes
## Frequency   156    9
## Proportion 0.945 0.055
## -----
## cyclobenzaprine
##      n missing distinct
##    165      0        2
##
## Value      no  yes
## Frequency   124   41
## Proportion 0.752 0.248
## -----
## methenamine
##      n missing distinct
##    165      0        2
##
## Value      no  yes
## Frequency   131   34
## Proportion 0.794 0.206
## -----
## phenazopyridine
##      n missing distinct
##    165      0        2
##
## Value      no  yes
## Frequency   116   49
## Proportion 0.703 0.297
## -----
## oxybutynin
##      n missing distinct
##    165      0        2
##
## Value      no  yes
## Frequency   140   25
## Proportion 0.848 0.152
## -----

```

2. 1,2 vs 3,4

A. Hypothesis Tests

```
ic_sensitivity$outcome <- with(ic_sensitivity, as.factor(ifelse(cases %in% c("1 Definite", "2 Possibly"),  
table(ic_sensitivity$outcome,useNA="always")
```

```
##  
##   no  yes <NA>  
## 158   7    0
```

Summary for Cases (Outcome = Yes)

```
describe(ic_sensitivity %>% filter(outcome=="yes") %>% select(-id,-ic_list))
```

```
## ic_sensitivity %>% filter(outcome == "yes") %>% select(-id, -ic_list)  
##  
## 15 Variables      7 Observations  
## -----  
## cases  
##      n missing distinct  
##      7      0        2  
##  
## Value      1 Definite 2 Possibly  
## Frequency           3        4  
## Proportion      0.429      0.571  
## -----  
## age_last_visit  
##      n missing distinct      Info      Mean      Gmd  
##      7      0        6    0.982    66.71    12.57  
##  
## Value      53      61      63      65      75      87  
## Frequency      1      1      2      1      1      1  
## Proportion 0.143 0.143 0.286 0.143 0.143 0.143  
## -----  
## gender  
##      n missing distinct  
##      7      0        2  
##  
## Value      1 Female  2 Male  
## Frequency      6      1  
## Proportion    0.857    0.143  
## -----  
## race  
##      n missing distinct  
##      7      0        3  
##  
## Value      1 White 2 Black 3 Other  
## Frequency      5      1      1  
## Proportion    0.714    0.143    0.143  
## -----  
## smoking
```

```

##      n missing distinct
##      7      0      2
##
## Value      1 Never 3 Former
## Frequency      6      1
## Proportion 0.857 0.143
## -----
## elmiron
##      n missing distinct
##      7      0      2
##
## Value      no  yes
## Frequency      3   4
## Proportion 0.429 0.571
## -----
## hydroxyzine
##      n missing distinct
##      7      0      2
##
## Value      no  yes
## Frequency      4   3
## Proportion 0.571 0.429
## -----
## tca
##      n missing distinct
##      7      0      2
##
## Value      no  yes
## Frequency      5   2
## Proportion 0.714 0.286
## -----
## gabapentin
##      n missing distinct
##      7      0      2
##
## Value      no  yes
## Frequency      4   3
## Proportion 0.571 0.429
## -----
## hydroxychloroquine
##      n missing distinct  value
##      7      0      1    no
##
## Value      no
## Frequency      7
## Proportion      1
## -----
## cyclobenzaprine
##      n missing distinct
##      7      0      2
##
## Value      no  yes
## Frequency      5   2
## Proportion 0.714 0.286

```

```
## -----
## methenamine
##      n missing distinct
##      7      0      2
##
## Value      no  yes
## Frequency    6   1
## Proportion 0.857 0.143
## -----
## phenazopyridine
##      n missing distinct
##      7      0      2
##
## Value      no  yes
## Frequency    4   3
## Proportion 0.571 0.429
## -----
## oxybutynin
##      n missing distinct
##      7      0      2
##
## Value      no  yes
## Frequency    5   2
## Proportion 0.714 0.286
## -----
## outcome
##      n missing distinct  value
##      7      0      1    yes
##
## Value      yes
## Frequency    7
## Proportion    1
## -----
```

Summary for Non-cases (Outcome = No)

```
describe(ic_sensitivity %>% filter(outcome=="no") %>% select(-id,-ic_list))
```

```
## ic_sensitivity %>% filter(outcome == "no") %>% select(-id, -ic_list)
##
## 15 Variables      158 Observations
## -----
## cases
##      n missing distinct
##     158      0      2
##
## Value      3 Not 4 No images
## Frequency    32     126
## Proportion   0.203    0.797
## -----
## age_last_visit
##      n missing distinct  Info  Mean  Gmd   .05   .10
##     158      0      58  0.999  61.23  17.99  35.7  39.0
```



```

##      .25      .50      .75      .90      .95
##    50.0    64.0    73.0    80.0    84.3
##
## lowest : 24 25 28 29 31, highest: 86 87 88 89 90
## -----
## gender
##      n missing distinct
##    158      0      2
##
## Value      1 Female      2 Male
## Frequency      142      16
## Proportion    0.899    0.101
## -----
## race
##      n missing distinct
##    158      0      3
##
## Value      1 White 2 Black 3 Other
## Frequency      110      38      10
## Proportion    0.696    0.241    0.063
## -----
## smoking
##      n missing distinct
##    150      8      3
##
## Value      1 Never 2 Current 3 Former
## Frequency      112      4      34
## Proportion    0.747    0.027    0.227
## -----
## elmiron
##      n missing distinct
##    158      0      2
##
## Value      no  yes
## Frequency    122   36
## Proportion 0.772 0.228
## -----
## hydroxyzine
##      n missing distinct
##    158      0      2
##
## Value      no  yes
## Frequency    122   36
## Proportion 0.772 0.228
## -----
## tca
##      n missing distinct
##    158      0      2
##
## Value      no  yes
## Frequency    112   46
## Proportion 0.709 0.291
## -----
## gabapentin

```

```

##      n missing distinct
##    158      0      2
##
## Value      no  yes
## Frequency   96  62
## Proportion 0.608 0.392
## -----
## hydroxychloroquine
##      n missing distinct
##    158      0      2
##
## Value      no  yes
## Frequency  149   9
## Proportion 0.943 0.057
## -----
## cyclobenzaprine
##      n missing distinct
##    158      0      2
##
## Value      no  yes
## Frequency  119  39
## Proportion 0.753 0.247
## -----
## methenamine
##      n missing distinct
##    158      0      2
##
## Value      no  yes
## Frequency  125  33
## Proportion 0.791 0.209
## -----
## phenazopyridine
##      n missing distinct
##    158      0      2
##
## Value      no  yes
## Frequency  112  46
## Proportion 0.709 0.291
## -----
## oxybutynin
##      n missing distinct
##    158      0      2
##
## Value      no  yes
## Frequency  135  23
## Proportion 0.854 0.146
## -----
## outcome
##      n missing distinct  value
##    158      0      1    no
##
## Value      no
## Frequency  158
## Proportion  1

```

```
## -----
```

Fisher's Exact Tests

Odds ratio values given here are “hypothesized odds ratio”- different from sample odds ratio which we typically report. Sample odds ratio given in next section

```
ic_sensitivity %>% select(-id,-ic_list,-cases,-outcome,-age_last_visit) %>%  
  apply(.,y= ic_sensitivity$outcome,function(x,y) fisher.test(y,x))
```

```
## $gender  
##  
## Fisher's Exact Test for Count Data  
##  
## data: y and x  
## p-value = 0.5398  
## alternative hypothesis: true odds ratio is not equal to 1  
## 95 percent confidence interval:  
## 0.03028728 13.42560678  
## sample estimates:  
## odds ratio  
## 1.475125  
##  
## $race  
##  
## Fisher's Exact Test for Count Data  
##  
## data: y and x  
## p-value = 0.6152  
## alternative hypothesis: two.sided  
##  
## $smoking  
##  
## Fisher's Exact Test for Count Data  
##  
## data: y and x  
## p-value = 1  
## alternative hypothesis: two.sided  
##  
## $elmiron  
##  
## Fisher's Exact Test for Count Data  
##  
## data: y and x  
## p-value = 0.05965  
## alternative hypothesis: true odds ratio is not equal to 1  
## 95 percent confidence interval:  
## 0.7198942 31.9082656  
## sample estimates:  
## odds ratio
```

```

## 4.466291
##
##
## $hydroxyzine
##
## Fisher's Exact Test for Count Data
##
## data: y and x
## p-value = 0.3576
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 0.3535386 15.6785414
## sample estimates:
## odds ratio
## 2.524431
##
##
## $tca
##
## Fisher's Exact Test for Count Data
##
## data: y and x
## p-value = 1
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 0.08969406 6.21420804
## sample estimates:
## odds ratio
## 0.9740496
##
##
## $gabapentin
##
## Fisher's Exact Test for Count Data
##
## data: y and x
## p-value = 1
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 0.1643564 7.1123540
## sample estimates:
## odds ratio
## 1.160219
##
##
## $hydroxychloroquine
##
## Fisher's Exact Test for Count Data
##
## data: y and x
## p-value = 1
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 0.00000 13.49227

```

```

## sample estimates:
## odds ratio
##      0
##
##
## $cyclobenzaprine
##
## Fisher's Exact Test for Count Data
##
## data:  y and x
## p-value = 1
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  0.1118345 7.8159694
## sample estimates:
## odds ratio
##  1.219004
##
##
## $methenamine
##
## Fisher's Exact Test for Count Data
##
## data:  y and x
## p-value = 1
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  0.01333047 5.50256741
## sample estimates:
## odds ratio
##  0.6328718
##
##
## $phenazopyridine
##
## Fisher's Exact Test for Count Data
##
## data:  y and x
## p-value = 0.4248
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  0.2563609 11.2140999
## sample estimates:
## odds ratio
##  1.818694
##
##
## $oxybutynin
##
## Fisher's Exact Test for Count Data
##
## data:  y and x
## p-value = 0.2868
## alternative hypothesis: true odds ratio is not equal to 1

```

```
## 95 percent confidence interval:
##    0.2102611 15.3242932
## sample estimates:
## odds ratio
##    2.332249
```

Levene's test for Equality of variance does not reject the null hypothesis (Variances are equal)

```
car::leveneTest(age_last_visit~outcome,data=ic_sensitivity)
```

```
## Levene's Test for Homogeneity of Variance (center = median)
##      Df F value Pr(>F)
## group  1  2.6374 0.1063
##      163
```

We will use Independent Two-sample T-test (Pooled) We do not reject the null hypothesis that age at last visit is different across the outcome group

```
t.test(age_last_visit~outcome,data=ic_sensitivity,var.equal=TRUE)
```

```
##
## Two Sample t-test
##
## data: age_last_visit by outcome
## t = -0.91062, df = 163, p-value = 0.3638
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
## -17.363404  6.403187
## sample estimates:
## mean in group no mean in group yes
##      61.23418      66.71429
```

```
with(ic_sensitivity,table(outcome,elmiron))
```

```
##      elmiron
## outcome no yes
##      no 122 36
##      yes  3  4
```

Sample Odds ratio

```
ic_sensitivity %>% select(-id,-ic_list,-cases,-outcome,-age_last_visit) %>%
  apply(.,y= ic_sensitivity$outcome,function(x,y) exp(coef(glm(y~x,family="binomial"))))
```

```
## $gender
## (Intercept)      x2 Male
## 0.04225352 1.47916667
##
## $race
## (Intercept)      x2 Black      x3 Other
```

```
## 0.04545455 0.57894737 2.20000000
##
## $smoking
## (Intercept) x2 Current x3 Former
## 5.357143e-02 4.387531e-07 5.490196e-01
##
## $elmiron
## (Intercept) xyes
## 0.02459016 4.51851852
##
## $hydroxyzine
## (Intercept) xyes
## 0.03278689 2.54166667
##
## $tca
## (Intercept) xyes
## 0.04464286 0.97391304
##
## $gabapentin
## (Intercept) xyes
## 0.04166667 1.16129032
##
## $hydroxychloroquine
## (Intercept) xyes
## 4.697987e-02 1.840548e-07
##
## $cyclobenzaprine
## (Intercept) xyes
## 0.04201681 1.22051282
##
## $methenamine
## (Intercept) xyes
## 0.0480000 0.6313131
##
## $phenazopyridine
## (Intercept) xyes
## 0.03571429 1.82608696
##
## $oxybutynin
## (Intercept) xyes
## 0.03703704 2.34782609
```

```
confint_glm <- function(x,y){
  mod <- glm(y~x,family="binomial")
  mod_df <- broom::tidy(mod)
  mod_df <- mod_df %>% mutate(lci = exp(estimate-1.96*std.error),
                             uci = exp(estimate+1.96*std.error)) %>%
    mutate(estimate = exp(estimate)) %>% select(term,estimate,lci,uci)
  print(mod_df)
}
```

```
ic_sensitivity %>% select(-id,-cases,-outcome,-ic_list) %>%
  sapply(.,y= ic_sensitivity$outcome,function(x,y) {confint_glm(x,y)})
```

```

## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.00921 0.000249 0.341
## 2 x          1.02    0.972    1.08
## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.0423 0.0187 0.0956
## 2 x2 Male     1.48    0.167 13.1
## # A tibble: 3 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.0455 0.0186 0.111
## 2 x2 Black    0.579 0.0655 5.11
## 3 x3 Other    2.20   0.234 20.7
## # A tibble: 3 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.0536    0.0236 0.122
## 2 x2 Current 0.000000439 0      Inf
## 3 x3 Former  0.549    0.0639 4.72
## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.0246 0.00782 0.0773
## 2 xyes       4.52    0.966 21.1
## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.0328 0.0121 0.0888
## 2 xyes       2.54    0.544 11.9
## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.0446 0.0182 0.109
## 2 xyes       0.974 0.182 5.20
## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.0417 0.0153 0.113
## 2 xyes       1.16    0.251 5.37
## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.0470    0.0220 0.100
## 2 xyes       0.000000184 0      Inf
## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl>    <dbl> <dbl>
## 1 (Intercept) 0.0420 0.0172 0.103
## 2 xyes       1.22    0.228 6.54
## # A tibble: 2 x 4
##   term      estimate    lci    uci

```



```

##      <chr>          <dbl> <dbl> <dbl>
## 1 (Intercept)    0.0480 0.0212 0.109
## 2 xyes           0.631  0.0734 5.43
## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl> <dbl> <dbl>
## 1 (Intercept)  0.0357 0.0132 0.0968
## 2 xyes        1.83   0.393  8.48
## # A tibble: 2 x 4
##   term      estimate    lci    uci
##   <chr>      <dbl> <dbl> <dbl>
## 1 (Intercept)  0.0370 0.0152 0.0904
## 2 xyes        2.35   0.430 12.8

##      age_last_visit gender      race      smoking      elmiron
## term      Character,2  Character,2 Character,3 Character,3 Character,2
## estimate Numeric,2    Numeric,2  Numeric,3  Numeric,3  Numeric,2
## lci      Numeric,2    Numeric,2  Numeric,3  Numeric,3  Numeric,2
## uci      Numeric,2    Numeric,2  Numeric,3  Numeric,3  Numeric,2
##      hydroxyzine tca      gabapentin hydroxychloroquine
## term      Character,2 Character,2 Character,2 Character,2
## estimate Numeric,2    Numeric,2  Numeric,2  Numeric,2
## lci      Numeric,2    Numeric,2  Numeric,2  Numeric,2
## uci      Numeric,2    Numeric,2  Numeric,2  Numeric,2
##      cyclobenzaprine methenamine phenazopyridine oxybutynin
## term      Character,2  Character,2 Character,2  Character,2
## estimate Numeric,2    Numeric,2  Numeric,2  Numeric,2
## lci      Numeric,2    Numeric,2  Numeric,2  Numeric,2
## uci      Numeric,2    Numeric,2  Numeric,2  Numeric,2

```