HST.953x Workshop 2.09: IAC Case Study

H. David Shea

16 Jul 2021

Contents

Description

This document contains the write up and code for my version of interpretation of the data from the study of whether indwelling arterial catheters (IAC) have any effect on patient mortality. The study objective was:

"To estimate the effect that administration of IAC during an ICU admission has on 28 day mortality in patients within the MIMIC II study who received mechanical ventilation, while adjusting for age, gender, severity of illness and comorbidities."

Base data set

Import dataset from **PhysioNet** - raw data file downloaded in previous exercise.

```
fnm <- fs::path(base_dir, "exercises/exploratory_data_analysis/aline_full_cohort_data.csv")
dat <- read.csv(fnm)
rm(fnm)

is01_factor_column <- function(x) {
  v <- unique(x[!is.na(x)])
  ((length(v) == 1) & (v[1] %in% c(0,1))) | ((length(v) == 2) & (v[1] %in% c(0,1)) & (v[2] %in% c(0,1)))
}

# convert to factors where appropriate
dat <- dat %>%
  mutate(across(where(is01_factor_column), as.factor))
dat$service_unit <- as.factor(dat$service_unit)
dat$day_icu_intime <- as.factor(dat$day_icu_intime)
```

Exploratory Data Analysis

Here we examine:

- full cohort characteristics
- chracteristics of IAC versus non-IAC parts of the cohort
- chracteristics of portion of the cohort who were alive after 28 days versus those who died

```
tab_full <- produce.table1(dat)
kable(tab_full, caption = "Full cohort characteristics")
```

Table 1: Full cohort characteristics

	Average (SD), or N (%)
aline_flg==1	984 (55.4%)
icu_los_day	3.3 (3.4)
hospital_los_day	8.1 (8.2)
age	54.4 (21.1)
gender_num==1	1025 (57.7%) [Missing: 1]
weight_first	80.1 (22.5) [Missing: 110]
bmi	27.8 (8.2) [Missing: 466]
sapsi_first	14.1 (4.1) [Missing: 85]
sofa_first	5.8 (2.3) [Missing: 6]
service_unit==SICU	982 (55.3%)
service_num==1	982 (55.3%)
day_icu_intime==Saturday	278 (15.7%)
day_icu_intime_num	4.1 (2)
hour_icu_intime	10.6 (7.9)
hosp_exp_flg==0	1532 (86.3%)
icu_exp_flg==0	1606 (90.4%)
day_28_flg==0	1493 (84.1%)
mort_day_censored	614.3 (403.1)
censor_flg==1	1279 (72%)
sepsis_flg==0	1776 (100%)
chf_flg==0	1563 (88%)
afib_flg==0	1569 (88.3%)
renal_flg==0	1716 (96.6%)
liver_flg==0	1677 (94.4%)
copd_flg==0	1619 (91.2%)
cad_flg==0	1653 (93.1%)
stroke_flg==0	1554 (87.5%)
mal_flg==0	1520 (85.6%)
resp_flg==0	1211 (68.2%)
map_1st	88.2 (17.6)
hr_1st	87.9 (18.8)
temp_1st	97.8 (4.5) [Missing: 3]
spo2_1st	98.4 (5.5)
abg_count	6 (8.7)
wbc_first	12.3 (6.6) [Missing: 8]
hgb_first	12.6 (2.2) [Missing: 8]
platelet_first	246.1 (99.9) [Missing: 8]
sodium_first	139.6 (4.7) [Missing: 5]

	Average (SD), or N (%)
potassium__first	4.1 (0.8) [Missing: 5]
tco2__first	24.4 (5) [Missing: 5]
chloride__first	103.8 (5.7) [Missing: 5]
bun__first	19.3 (14.4) [Missing: 5]
creatinine__first	1.1 (1.1) [Missing: 6]
po2__first	227.6 (144.9) [Missing: 186]
pco2__first	43.4 (14) [Missing: 186]
iv__day_1	1622.9 (1677.1) [Missing: 143]

```r
dat_by_aline <- split(dat, dat$aline_flg)
labs <- attr(produce.table1(dat_by_aline[[1]]), "labels")
tab_by_aline <- cbind(
  produce.table1(dat_by_aline[[1]], labels = labs),
  produce.table1(dat_by_aline[[2]], labels = labs)
)
colnames(tab_by_aline) <- paste0("Average (SD), or N (%), ", c("No IAC", "IAC"))
kable(tab_by_aline, caption = "Patient characteristics stratified by IAC administration")
```

Table 2: Patient characteristics stratified by IAC administration

	Average (SD), or N (%), No IAC	Average (SD), or N (%), IAC
aline__flg==0	792 (100%)	0 (0%)
icu__los__day	2.1 (1.9)	4.3 (3.9)
hospital__los__day	5.4 (5.4)	10.3 (9.3)
age	53 (21.7)	55.5 (20.5)
gender__num==1	447 (56.5%) [Missing: 1]	578 (58.7%)
weight__first	79.2 (22.6) [Missing: 71]	80.7 (22.4) [Missing: 39]
bmi	28 (9.1) [Missing: 220]	27.7 (7.5) [Missing: 246]
sapsi__first	12.7 (3.8) [Missing: 70]	15.2 (4) [Missing: 15]
sofa__first	4.8 (2.1) [Missing: 4]	6.6 (2.2) [Missing: 2]
service__unit==MICU	480 (60.6%)	252 (25.6%)
service__num==0	504 (63.6%)	290 (29.5%)
day__icu__intime==Saturday	138 (17.4%)	140 (14.2%)
day__icu__intime__num	4 (2)	4.1 (2)
hour__icu__intime	9.9 (7.7)	11.2 (8.1)
hosp__exp__flg==0	702 (88.6%)	830 (84.3%)
icu__exp__flg==0	734 (92.7%)	872 (88.6%)
day__28__flg==0	679 (85.7%)	814 (82.7%)
mort__day__censored	619.1 (388.3)	610.5 (414.8)
censor__flg==1	579 (73.1%)	700 (71.1%)
sepsis__flg==0	792 (100%)	984 (100%)
chf__flg==0	695 (87.8%)	868 (88.2%)
afib__flg==0	710 (89.6%)	859 (87.3%)
renal__flg==0	764 (96.5%)	952 (96.7%)
liver__flg==0	754 (95.2%)	923 (93.8%)
copd__flg==0	711 (89.8%)	908 (92.3%)
cad__flg==0	741 (93.6%)	912 (92.7%)
stroke__flg==0	722 (91.2%)	832 (84.6%)
mal__flg==0	700 (88.4%)	820 (83.3%)
resp__flg==0	514 (64.9%)	697 (70.8%)

	Average (SD), or N (%), No IAC	Average (SD), or N (%), IAC
map_1st	87.5 (15.9)	88.9 (18.8)
hr_1st	88.4 (18.8)	87.5 (18.7)
temp_1st	97.9 (3.8) [Missing: 3]	97.7 (5.1)
spo2_1st	98.4 (5.7)	98.5 (5.4)
abg_count	1.4 (1.6)	9.7 (10.2)
wbc_first	11.7 (6.5) [Missing: 6]	12.8 (6.6) [Missing: 2]
hgb_first	12.7 (2.2) [Missing: 6]	12.4 (2.2) [Missing: 2]
platelet_first	254.3 (104.5) [Missing: 6]	239.5 (95.6) [Missing: 2]
sodium_first	139.8 (4.8) [Missing: 3]	139.4 (4.7) [Missing: 2]
potassium_first	4.1 (0.8) [Missing: 3]	4.1 (0.8) [Missing: 2]
tco2_first	24.7 (4.9) [Missing: 3]	24.2 (5.1) [Missing: 2]
chloride_first	103.3 (5.4) [Missing: 3]	104.3 (5.9) [Missing: 2]
bun_first	18.9 (14.5) [Missing: 3]	19.6 (14.3) [Missing: 2]
creatinine_first	1.1 (1.2) [Missing: 4]	1.1 (1) [Missing: 2]
po2_first	223.8 (152.9) [Missing: 178]	230.1 (139.6) [Missing: 8]
pco2_first	44.9 (15.9) [Missing: 178]	42.5 (12.5) [Missing: 8]
iv_day_1	1364.2 (1406.8) [Missing: 110]	1808.4 (1825) [Missing: 33]

```r
dat_by_28day <- split(dat, dat$day_28_flg)
labs <- attr(produce.table1(dat_by_28day[[1]]), "labels")
tab_by_28day <- cbind(
  produce.table1(dat_by_28day[[1]], labels = labs),
  produce.table1(dat_by_28day[[2]], labels = labs)
)
colnames(tab_by_28day) <- paste0("Average (SD), or N (%), ", c("Alive", "Dead"))
kable(tab_by_28day, caption = "Patient characteristics stratified by 28 day mortality")
```

Table 3: Patient characteristics stratified by 28 day mortality

	Average (SD), or N (%), Alive	Average (SD), or N (%), Dead
aline_flg==1	814 (54.5%)	170 (60.1%)
icu_los_day	3.2 (3.2)	4 (4)
hospital_los_day	8.4 (8.4)	6.4 (6.4)
age	50.8 (20.1)	73.3 (15.3)
gender_num==1	886 (59.4%) [Missing: 1]	139 (49.1%)
weight_first	81.4 (22.7) [Missing: 77]	72.4 (19.9) [Missing: 33]
bmi	28.2 (8.3) [Missing: 392]	26 (7.2) [Missing: 74]
sapsi_first	13.6 (3.9) [Missing: 51]	17.3 (3.8) [Missing: 34]
sofa_first	5.7 (2.3) [Missing: 3]	6.6 (2.4) [Missing: 3]
service_unit==SICU	829 (55.5%)	153 (54.1%)
service_num==1	829 (55.5%)	153 (54.1%)
day_icu_intime==Saturday	235 (15.7%)	43 (15.2%)
day_icu_intime_num	4 (2)	4.1 (2)
hour_icu_intime	10.5 (7.9)	11 (8)
hosp_exp_flg==0	1490 (99.8%)	42 (14.8%)
icu_exp_flg==0	1493 (100%)	113 (39.9%)
day_28_flg==0	1493 (100%)	0 (0%)
mort_day_censored	729.6 (331.4)	6.1 (6.4)
censor_flg==1	1279 (85.7%)	0 (0%)
sepsis_flg==0	1493 (100%)	283 (100%)

	Average (SD), or N (%), Alive	Average (SD), or N (%), Dead
chf_flg==0	1348 (90.3%)	215 (76%)
afib_flg==0	1372 (91.9%)	197 (69.6%)
renal_flg==0	1447 (96.9%)	269 (95.1%)
liver_flg==0	1413 (94.6%)	264 (93.3%)
copd_flg==0	1377 (92.2%)	242 (85.5%)
cad_flg==0	1403 (94%)	250 (88.3%)
stroke_flg==0	1386 (92.8%)	168 (59.4%)
mal_flg==0	1294 (86.7%)	226 (79.9%)
resp_flg==0	1056 (70.7%)	155 (54.8%)
map_1st	88.2 (17.5)	88.3 (17.9)
hr_1st	88.3 (18.4)	85.8 (20.6)
temp_1st	97.8 (4.6) [Missing: 1]	97.7 (4.5) [Missing: 2]
spo2_1st	98.6 (5)	97.8 (7.6)
abg_count	5.7 (7.7)	7.5 (12.5)
wbc_first	12.2 (6.4) [Missing: 6]	12.7 (7.5) [Missing: 2]
hgb_first	12.7 (2.2) [Missing: 6]	11.9 (2.1) [Missing: 2]
platelet_first	246.8 (97.3) [Missing: 6]	242.1 (112.6) [Missing: 2]
sodium_first	139.6 (4.6) [Missing: 4]	139.1 (5.4) [Missing: 1]
potassium_first	4.1 (0.8) [Missing: 4]	4.2 (0.9) [Missing: 1]
tco2_first	24.3 (4.8) [Missing: 4]	25 (5.8) [Missing: 1]
chloride_first	104.1 (5.6) [Missing: 4]	102.6 (6.4) [Missing: 1]
bun_first	18 (12.9) [Missing: 4]	26.2 (19) [Missing: 1]
creatinine_first	1.1 (1.1) [Missing: 5]	1.2 (0.9) [Missing: 1]
po2_first	231.3 (146.3) [Missing: 153]	207.9 (135.8) [Missing: 33]
pco2_first	43.3 (12.9) [Missing: 153]	43.8 (18.6) [Missing: 33]
iv_day_1	1694.2 (1709.5) [Missing: 127]	1258 (1449.4) [Missing: 16]

Basic Mortality Analysis

In the tables above, we see that 170 of the 984 (17.2 %) subjects receiving IAC died within 28 days, whereas 113 of 792 (14.2 %) died within 28 days in the no-IAC group. In a univariate analysis, we can assess if the lower rate of mortality is statistically significant by fitting a single covariate `aline_flg` logistic regression.

Note: All of the variables that we will use in the following analyses are binary or categorical except for age and the disease severity indicators (`sapsi_first` and `sofa_first`) which are continuous. While, our previous work does show that age has a linear relation to 28 day mortality, it has also shown that SAPS and SOFA scores do not. These will be converted to categorical variables for the analysis.

```
dat$sapsi_cat <- cut2(dat$sapsi_first, g = 5)
dat$sofa_cat <- cut2(dat$sofa_first, g = 5)

mort.glm <- glm(day_28_flg ~ aline_flg, data = dat, family = "binomial")

exp(mort.glm$coef[-1])
#> aline_flg1
#>   1.254919

exp(confint(mort.glm)[-1,])
#>    2.5 %    97.5 %
#> 0.9701035 1.6285165
```

```
summary(mort.glm)$coef
#>               Estimate Std. Error    z value      Pr(>|z|)
#> (Intercept) -1.7932333  0.1015988 -17.650149 1.014880e-69
#> aline_flg1   0.2270714  0.1320347   1.719786 8.547142e-02
```

The part of the cohort who received IAC had over a 25% increase in odds of 28 day mortality when compared to those who did not receive IAC. However, the confidence interval includes one (`ln(1) == 0`), so we would expect the p-value would be >0.05 which indeed shows in the coefficient summary for `aline_flg` at about 0.09.

As seen in the exploratory analyses, there are likely several important covariates that differed among those who received IAC and those who did not which may serve as confounders which could impact the view from this univariate analysis depending on the situation.

We will employ backwards step-wise elimination to get a better feel for the potential impact of confounding variables.

Step-wise Elimination

The variables under consideration for a full model are `aline_flg`, `age`, `gender_num`, disease severity indications (`sapsi_first`, `sofa_first`), ICU service type (`service_unit`), and comorbidities (`chf_flg`, `afib_flg`, `renal_flg`, `liver_flg`, `copd_flg`, `cad_flg`, `stroke_flg`, `mal_flg` and `resp_flg`).

```
mort.full.glm <- glm(day_28_flg ~ aline_flg + age + gender_num + sapsi_cat +
                        sofa_cat + service_unit + chf_flg + afib_flg + renal_flg +
                        liver_flg + copd_flg + cad_flg + stroke_flg + mal_flg + resp_flg,
                     data = dat, family = "binomial")

summary(mort.full.glm)
#>
#> Call:
#> glm(formula = day_28_flg ~ aline_flg + age + gender_num + sapsi_cat +
#>     sofa_cat + service_unit + chf_flg + afib_flg + renal_flg +
#>     liver_flg + copd_flg + cad_flg + stroke_flg + mal_flg + resp_flg,
#>     family = "binomial", data = dat)
#>
#> Deviance Residuals:
#>     Min       1Q   Median       3Q      Max
#> -2.2912  -0.4710  -0.2330  -0.1104   2.9640
#>
#> Coefficients:
#>                  Estimate Std. Error z value Pr(>|z|)
#> (Intercept)      -7.61471    0.86262  -8.827  < 2e-16 ***
#> aline_flg1        0.01085    0.20443   0.053 0.957679
#> age               0.04020    0.00627   6.412 1.44e-10 ***
#> gender_num1       0.16214    0.17296   0.937 0.348527
#> sapsi_cat[12,14)  0.36961    0.40348   0.916 0.359637
#> sapsi_cat[14,16)  1.01794    0.36214   2.811 0.004940 **
#> sapsi_cat[16,19)  0.92803    0.36794   2.522 0.011662 *
#> sapsi_cat[19,32]  1.77615    0.37446   4.743 2.10e-06 ***
#> sofa_cat5         0.49761    0.30267   1.644 0.100159
#> sofa_cat6         0.58530    0.30300   1.932 0.053396 .
#> sofa_cat[7, 9)    0.68011    0.29439   2.310 0.020876 *
```

```
#> sofa_cat[9,17]     0.75134     0.34062   2.206 0.027397 *
#> service_unitMICU   1.08086     0.67839   1.593 0.111100
#> service_unitSICU   0.64257     0.67144   0.957 0.338562
#> chf_flg1           0.23350     0.23381   0.999 0.317962
#> afib_flg1          0.52408     0.21122   2.481 0.013092 *
#> renal_flg1        -0.76796     0.40904  -1.877 0.060452 .
#> liver_flg1         0.47238     0.34032   1.388 0.165125
#> copd_flg1          0.23440     0.24631   0.952 0.341287
#> cad_flg1          -0.25674     0.28823  -0.891 0.373065
#> stroke_flg1        2.04301     0.21966   9.301   < 2e-16 ***
#> mal_flg1           0.49319     0.20897   2.360 0.018274 *
#> resp_flg1          0.69330     0.19166   3.617 0.000298 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
#>
#> (Dispersion parameter for binomial family taken to be 1)
#>
#>     Null deviance: 1400.58  on 1683  degrees of freedom
#> Residual deviance:  954.39  on 1661  degrees of freedom
#>   (92 observations deleted due to missingness)
#> AIC: 1000.4
#>
#> Number of Fisher Scoring iterations: 6
```

Now we use `drop1` with a Chi-square test to determine the variable with the least significance (i.e., highest Pr(>Chi) p-value) .

```
drop1(mort.full.glm, test = "Chisq")
#> Single term deletions
#>
#> Model:
#> day_28_flg ~ aline_flg + age + gender_num + sapsi_cat + sofa_cat +
#>     service_unit + chf_flg + afib_flg + renal_flg + liver_flg +
#>     copd_flg + cad_flg + stroke_flg + mal_flg + resp_flg
#>              Df Deviance     AIC    LRT  Pr(>Chi)
#> <none>            954.39 1000.39
#> aline_flg     1   954.39  998.39  0.003 0.9576771
#> age           1  1000.60 1044.60 46.210 1.063e-11 ***
#> gender_num    1   955.27  999.27  0.883 0.3475044
#> sapsi_cat     4   989.69 1027.69 35.304 4.023e-07 ***
#> sofa_cat      4   960.95  998.95  6.558 0.1611514
#> service_unit  2   960.11 1002.11  5.716 0.0573820 .
#> chf_flg       1   955.38  999.38  0.990 0.3196816
#> afib_flg      1   960.47 1004.47  6.080 0.0136708 *
#> renal_flg     1   958.20 1002.20  3.814 0.0508182 .
#> liver_flg     1   956.23 1000.23  1.839 0.1750410
#> copd_flg      1   955.28  999.28  0.893 0.3445691
#> cad_flg       1   955.20  999.20  0.811 0.3678829
#> stroke_flg    1  1045.22 1089.22 90.831 < 2.2e-16 ***
#> mal_flg       1   959.80 1003.80  5.410 0.0200201 *
#> resp_flg      1   967.57 1011.57 13.177 0.0002834 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

While `aline_flg` has the largest *p*-value, this variable is our primary discriminator for the study, so we drop the variable with the next highest *p*-value `cad_flg` the coronary artery disease indicator variable.

```
mort.d1.glm <- update(mort.full.glm, .~. - cad_flg)

drop1(mort.d1.glm, test = "Chisq")
#> Single term deletions
#>
#> Model:
#> day_28_flg ~ aline_flg + age + gender_num + sapsi_cat + sofa_cat +
#>     service_unit + chf_flg + afib_flg + renal_flg + liver_flg +
#>     copd_flg + stroke_flg + mal_flg + resp_flg
#>              Df Deviance     AIC    LRT   Pr(>Chi)
#> <none>            955.20  999.20
#> aline_flg     1   955.20  997.20   0.002 0.9674503
#> age           1  1000.92 1042.92  45.715 1.368e-11 ***
#> gender_num    1   955.98  997.98   0.784 0.3760520
#> sapsi_cat     4   990.38 1026.38  35.180 4.266e-07 ***
#> sofa_cat      4   961.75  997.75   6.552 0.1615399
#> service_unit  2   960.98 1000.98   5.782 0.0555160 .
#> chf_flg       1   955.92  997.92   0.719 0.3965762
#> afib_flg      1   961.32 1003.32   6.115 0.0134006 *
#> renal_flg     1   959.97 1001.97   4.774 0.0288966 *
#> liver_flg     1   957.06  999.06   1.862 0.1723427
#> copd_flg      1   956.02  998.02   0.824 0.3640764
#> stroke_flg    1  1045.73 1087.73  90.526 < 2.2e-16 ***
#> mal_flg       1   960.64 1002.64   5.435 0.0197326 *
#> resp_flg      1   968.84 1010.84  13.638 0.0002217 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

The following are the remaining iterations until only *p*-values < 0.05 exist.

`chf_flg` the congestive heart failure indicator variable.

```
mort.d2.glm <- update(mort.d1.glm, .~. - chf_flg)

drop1(mort.d2.glm, test = "Chisq")
#> Single term deletions
#>
#> Model:
#> day_28_flg ~ aline_flg + age + gender_num + sapsi_cat + sofa_cat +
#>     service_unit + afib_flg + renal_flg + liver_flg + copd_flg +
#>     stroke_flg + mal_flg + resp_flg
#>              Df Deviance     AIC    LRT   Pr(>Chi)
#> <none>            955.92  997.92
#> aline_flg     1   955.93  995.93   0.016 0.9003547
#> age           1  1005.90 1045.90  49.976 1.556e-12 ***
#> gender_num    1   956.65  996.65   0.734 0.3916088
#> sapsi_cat     4   991.04 1025.04  35.121 4.387e-07 ***
#> sofa_cat      4   962.39  996.39   6.467 0.1669071
#> service_unit  2   962.45 1000.45   6.529 0.0382253 *
#> afib_flg      1   963.01 1003.01   7.090 0.0077512 **
#> renal_flg     1   960.24 1000.24   4.321 0.0376445 *
```

```
#> liver_flg     1    957.70  997.70   1.780 0.1821692
#> copd_flg      1    956.95  996.95   1.035 0.3088774
#> stroke_flg    1   1045.73 1085.73  89.808 < 2.2e-16 ***
#> mal_flg       1    961.15 1001.15   5.231 0.0221921 *
#> resp_flg      1    970.13 1010.13  14.214 0.0001632 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

gender_num the patient gender indicator variable (1 = male; 0 = female).

```
mort.d3.glm <- update(mort.d2.glm, .~. - gender_num)

drop1(mort.d3.glm, test = "Chisq")
#> Single term deletions
#>
#> Model:
#> day_28_flg ~ aline_flg + age + sapsi_cat + sofa_cat + service_unit +
#>     afib_flg + renal_flg + liver_flg + copd_flg + stroke_flg +
#>     mal_flg + resp_flg
#>              Df Deviance     AIC    LRT  Pr(>Chi)
#> <none>            956.68  996.68
#> aline_flg     1   956.69  994.69  0.012 0.9118049
#> age           1  1005.94 1043.94 49.260 2.242e-12 ***
#> sapsi_cat     4   991.25 1023.25 34.570 5.693e-07 ***
#> sofa_cat      4   963.63  995.63  6.948 0.1386390
#> service_unit  2   962.97  998.97  6.295 0.0429508 *
#> afib_flg      1   963.78 1001.78  7.100 0.0077104 **
#> renal_flg     1   960.74  998.74  4.063 0.0438391 *
#> liver_flg     1   958.42  996.42  1.745 0.1865001
#> copd_flg      1   957.75  995.75  1.070 0.3009006
#> stroke_flg    1  1045.79 1083.79 89.109 < 2.2e-16 ***
#> mal_flg       1   961.82  999.82  5.143 0.0233462 *
#> resp_flg      1   970.91 1008.91 14.230 0.0001618 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

opd_flg the chronic obstructive pulmonary disease indicator variable.

```
mort.d4.glm <- update(mort.d3.glm, .~. - copd_flg)

drop1(mort.d4.glm, test = "Chisq")
#> Single term deletions
#>
#> Model:
#> day_28_flg ~ aline_flg + age + sapsi_cat + sofa_cat + service_unit +
#>     afib_flg + renal_flg + liver_flg + stroke_flg + mal_flg +
#>     resp_flg
#>            Df Deviance     AIC    LRT  Pr(>Chi)
#> <none>          957.75  995.75
#> aline_flg   1   957.76  993.76  0.013   0.90760
#> age         1  1011.03 1047.03 53.281 2.892e-13 ***
#> sapsi_cat   4   992.01 1022.01 34.260 6.590e-07 ***
#> sofa_cat    4   964.82  994.82  7.068   0.13233
```

```
#> service_unit  2   964.79  998.79  7.042   0.02957 *
#> afib_flg      1   965.06 1001.06  7.315   0.00684 **
#> renal_flg     1   961.63  997.63  3.882   0.04881 *
#> liver_flg     1   959.36  995.36  1.616   0.20366
#> stroke_flg    1  1045.88 1081.88 88.128 < 2.2e-16 ***
#> mal_flg       1   963.19  999.19  5.443   0.01965 *
#> resp_flg      1   973.07 1009.07 15.321 9.071e-05 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

liver_flg the liver disease indicator variable.

```
mort.d5.glm <- update(mort.d4.glm, .~. - liver_flg)

drop1(mort.d5.glm, test = "Chisq")
#> Single term deletions
#>
#> Model:
#> day_28_flg ~ aline_flg + age + sapsi_cat + sofa_cat + service_unit +
#>     afib_flg + renal_flg + stroke_flg + mal_flg + resp_flg
#>              Df Deviance     AIC    LRT  Pr(>Chi)
#> <none>            959.36  995.36
#> aline_flg     1   959.37  993.37  0.004 0.9494798
#> age           1  1012.75 1046.75 53.387 2.739e-13 ***
#> sapsi_cat     4   992.82 1020.82 33.454 9.642e-07 ***
#> sofa_cat      4   968.00  996.00  8.635 0.0708986 .
#> service_unit  2   966.59  998.59  7.225 0.0269877 *
#> afib_flg      1   966.38 1000.38  7.016 0.0080805 **
#> renal_flg     1   963.76  997.76  4.397 0.0360057 *
#> stroke_flg    1  1046.28 1080.28 86.916 < 2.2e-16 ***
#> mal_flg       1   964.82  998.82  5.454 0.0195198 *
#> resp_flg      1   973.97 1007.97 14.605 0.0001326 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

sofa_cat the SOFA score category variable.

```
mort.d6.glm <- update(mort.d5.glm, .~. - sofa_cat)

drop1(mort.d6.glm, test = "Chisq")
#> Single term deletions
#>
#> Model:
#> day_28_flg ~ aline_flg + age + sapsi_cat + service_unit + afib_flg +
#>     renal_flg + stroke_flg + mal_flg + resp_flg
#>              Df Deviance     AIC    LRT  Pr(>Chi)
#> <none>            980.16 1008.2
#> aline_flg     1   980.96 1007.0  0.796  0.372189
#> age           1  1029.59 1055.6 49.427 2.059e-12 ***
#> sapsi_cat     4  1030.70 1050.7 50.536 2.790e-10 ***
#> service_unit  2   987.11 1011.1  6.952  0.030928 *
#> afib_flg      1   987.59 1013.6  7.429  0.006418 **
#> renal_flg     1   983.34 1009.3  3.181  0.074508 .
```

```
#> stroke_flg    1   1069.67 1095.7 89.507 < 2.2e-16 ***
#> mal_flg       1    987.36 1013.4  7.197  0.007304 **
#> resp_flg      1    999.73 1025.7 19.575 9.673e-06 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

renal_flg the chronic renal disease indicator variable.

```
mort.d7.glm <- update(mort.d6.glm, .~. - renal_flg)

drop1(mort.d7.glm, test = "Chisq")
#> Single term deletions
#>
#> Model:
#> day_28_flg ~ aline_flg + age + sapsi_cat + service_unit + afib_flg +
#>     stroke_flg + mal_flg + resp_flg
#>              Df Deviance    AIC    LRT  Pr(>Chi)
#> <none>            983.34 1009.3
#> aline_flg     1   983.96 1008.0  0.619  0.431272
#> age           1  1031.03 1055.0 47.692 4.987e-12 ***
#> sapsi_cat     4  1033.11 1051.1 49.773 4.028e-10 ***
#> service_unit  2   989.10 1011.1  5.756  0.056239 .
#> afib_flg      1   989.74 1013.7  6.397  0.011434 *
#> stroke_flg    1  1074.38 1098.4 91.035 < 2.2e-16 ***
#> mal_flg       1   990.81 1014.8  7.466  0.006288 **
#> resp_flg      1  1003.89 1027.9 20.553 5.799e-06 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

service_unit the type of ICU service unit indicator variable.

```
mort.d8.glm <- update(mort.d7.glm, .~. - service_unit)

drop1(mort.d8.glm, test = "Chisq")
#> Single term deletions
#>
#> Model:
#> day_28_flg ~ aline_flg + age + sapsi_cat + afib_flg + stroke_flg +
#>     mal_flg + resp_flg
#>            Df Deviance    AIC    LRT  Pr(>Chi)
#> <none>          989.10 1011.1
#> aline_flg   1   989.10 1009.1  0.001  0.977380
#> age         1  1037.65 1057.7 48.556 3.209e-12 ***
#> sapsi_cat   4  1037.88 1051.9 48.788 6.465e-10 ***
#> afib_flg    1   995.60 1015.6  6.502  0.010777 *
#> stroke_flg  1  1078.58 1098.6 89.485 < 2.2e-16 ***
#> mal_flg     1   997.37 1017.4  8.274  0.004021 **
#> resp_flg    1  1022.30 1042.3 33.200 8.317e-09 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Final Model

```
mort.final.glm <- mort.d8.glm

summary(mort.final.glm)
#>
#> Call:
#> glm(formula = day_28_flg ~ aline_flg + age + sapsi_cat + afib_flg +
#>     stroke_flg + mal_flg + resp_flg, family = "binomial", data = dat)
#>
#> Deviance Residuals:
#>    Min      1Q   Median      3Q     Max
#> -2.3025  -0.4928  -0.2433  -0.1289   3.1103
#>
#> Coefficients:
#>                   Estimate Std. Error z value Pr(>|z|)
#> (Intercept)      -6.081944   0.445625 -13.648  < 2e-16 ***
#> aline_flg1        0.005078   0.179090   0.028  0.97738
#> age               0.037205   0.005644   6.592 4.33e-11 ***
#> sapsi_cat[12,14)  0.302084   0.391502   0.772  0.44035
#> sapsi_cat[14,16)  1.127302   0.344670   3.271  0.00107 **
#> sapsi_cat[16,19)  1.030901   0.347842   2.964  0.00304 **
#> sapsi_cat[19,32]  1.883738   0.347311   5.424 5.84e-08 ***
#> afib_flg1         0.522664   0.203485   2.569  0.01021 *
#> stroke_flg1       1.870553   0.199980   9.354  < 2e-16 ***
#> mal_flg1          0.592458   0.202297   2.929  0.00340 **
#> resp_flg1         0.976808   0.171629   5.691 1.26e-08 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
#>
#> (Dispersion parameter for binomial family taken to be 1)
#>
#>     Null deviance: 1413.4  on 1690  degrees of freedom
#> Residual deviance:  989.1  on 1680  degrees of freedom
#>   (85 observations deleted due to missingness)
#> AIC: 1011.1
#>
#> Number of Fisher Scoring iterations: 6

mort_final_tab <- cbind(round(exp(mort.final.glm$coef[-1]), 2),
                        round(exp(confint(mort.final.glm)[-1,]), 2),
                        round(summary(mort.final.glm)$coefficients[-1, 4], 3))
rownames(mort_final_tab) <-
  c(
    "IAC",
    "Age (per year increase)",
    "SAPSI [12-14)* (relative to SAPSI <12)",
    "SAPSI [14-16)*",
    "SAPSI [16-19)*",
    "SAPSI [19-32]*",
    "Atrial fibrillation",
    "Stroke",
    "Malignancy",
    "Non-COPD respiratory disease"
  )
```

```r
colnames(mort_final_tab) <-
  c("AOR", "Lower 95% CI", "Upper 95% CI", "p-value")
kable(mort_final_tab,
      caption = "Multivariable logistic regression analysis for mortality at 28 days outcome (final mode
```

Table 4: Multivariable logistic regression analysis for mortality at 28 days outcome (final model)

	AOR	Lower 95% CI	Upper 95% CI	p-value
IAC	1.01	0.71	1.43	0.977
Age (per year increase)	1.04	1.03	1.05	0.000
SAPSI [12–14)* (relative to SAPSI <12)	1.35	0.63	2.97	0.440
SAPSI [14–16)*	3.09	1.61	6.28	0.001
SAPSI [16–19)*	2.80	1.45	5.74	0.003
SAPSI [19–32]*	6.58	3.42	13.46	0.000
Atrial fibrillation	1.69	1.13	2.51	0.010
Stroke	6.49	4.40	9.64	0.000
Malignancy	1.81	1.21	2.68	0.003
Non-COPD respiratory disease	2.66	1.90	3.73	0.000