

## Example analysis (Stata version)

```

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  _/ _/ _/ _/ _/

17.0
MP-Parallel Edition

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Notes:
  1. Unicode is supported; see help unicode_advice.
  2. More than 2 billion observations are allowed; see help obs_advice.
  3. Maximum number of variables is set to 5,000; see help set maxvar.

```

## Read in data

## Flag first ICULOS per patient

```
In [3]: %stata
sort patid iculos
egen patid fl = tag(patid)
```

```
. sort patid iculos

. egen patid_fl = tag(patid)

.
```

## What's in the dataset

In [4]: `%%stata`  
describe

Contains data from ../data/icu\_data.dta

Observations: 1,201,974

Variables: 14

3 Mar 2020 08:58

Variable name	Storage type	Display format	Value label	Variable label
age	float	%9.0g		Age (years)
gender	byte	%8.0g		Gender
iculos	int	%8.0g		ICU length-of-stay (hours since ICU admission)
hr	double	%10.0g		Heart rate (beats per minute)
temp	double	%10.0g		Temperature (Deg C)
sbp	double	%10.0g		Systolic BP (mm Hg)
dbp	double	%10.0g		Diastolic BP (mm Hg)
resp	double	%10.0g		Respiration rate (breaths per minute)
o2sat	double	%10.0g		Pulse oximetry (%)
map	double	%10.0g		Mean arterial pressure (mm Hg)
sepsislabel	byte	%8.0g		SepsisLabel
hospid	str1	%9s		Hospital ID
patid	float	%9.0g		Patient ID
patid_fl	byte	%8.0g		tag(patid)

Sorted by: patid iculos

Note: Dataset has changed since last saved.

## Distributions of each of the variables

In [5]: `%%stata`  
codebook

---

age	Age (years)
-----	-------------

---

Type: Numeric (float)

Range: [14,100]

Units: .01

Unique values: 5,242

Missing .: 0/1,201,974

Mean: 61.7395

Std. dev.: 16.5491

Percentiles:	10%	25%	50%	75%	90%
	38.6	51	63.44	74	82

---

gender	Gender
--------	--------

---

Type: Numeric (byte)

Range: [0,1]

Units: 1

Unique values: 2

Missing .: 0/1,201,974

Tabulation:	Freq.	Value
	542,654	0
	659,320	1

---

iculos	ICU length-of-stay (hours since ICU admission)
--------	--

---

Type: Numeric (int)

Range: [1,336]

Units: 1

Unique values: 336

Missing .: 0/1,201,974

Mean: 26.1779

Std. dev.: 27.9166

Percentiles:	10%	25%	50%	75%	90%
	4	10	21	34	46

---

hr	Heart rate (beats per minute)
----	-------------------------------

---

Type: Numeric (double)

Range: [20,223]

Units: .01

Unique values: 333

Missing .: 131,167/1,201,974

Mean: 84.2342

Std. dev.: 17.5981

Percentiles:	10%	25%	50%	75%	90%
	62	72	83	95.5	107.5

---

temp	Temperature (Deg C)
------	---------------------

---

Type: Numeric (double)

Range: [20.9,50]  
Unique values: 581

Units: .01  
Missing .: 822,321/1,201,974

Mean: 36.9422  
Std. dev.: .758753

Percentiles:	10%	25%	50%	75%	90%
	36.06	36.5	36.9	37.4	37.9

sbp

Systolic BP (mm Hg)

Type: Numeric (double)

Range: [20,298]  
Unique values: 926

Units: .01  
Missing .: 176,747/1,201,974

Mean: 124.674  
Std. dev.: 23.6316

Percentiles:	10%	25%	50%	75%	90%
	96	107	122	140	156

dbp

Diastolic BP (mm Hg)

Type: Numeric (double)

Range: [20,300]  
Unique values: 653

Units: .01  
Missing .: 373,178/1,201,974

Mean: 64.9574  
Std. dev.: 14.1525

Percentiles:	10%	25%	50%	75%	90%
	49	55	63	73	83

resp

Respiration rate (breaths per minute)

Type: Numeric (double)

Range: [1,100]  
Unique values: 223

Units: .01  
Missing .: 205,042/1,201,974

Mean: 18.7334  
Std. dev.: 5.02104

Percentiles:	10%	25%	50%	75%	90%
	13	16	18	21	25

o2sat

Pulse oximetry (%)

Type: Numeric (double)

Range: [20,100]  
Unique values: 145

Units: .1  
Missing .: 170,544/1,201,974

Mean: 97.1494  
Std. dev.: 2.97941

Percentiles:	10%	25%	50%	75%	90%
	94	96	98	99	100

map

Mean arterial pressure (mm Hg)

Type: Numeric (double)

Range: [20,300]	Units: .01
Unique values: 905	Missing .: 163,352/1,201,974

Mean: 83.5463  
Std. dev.: 16.5921

Percentiles:	10%	25%	50%	75%	90%
	64.5	72	82	93	105

sepsislabel

SepsisLabel

Type: Numeric (byte)

Range: [0,1]	Units: 1
Unique values: 2	Missing .: 0/1,201,974

Tabulation: Freq.	Value
1,200,317	0
1,657	1

hospid

Hospital ID

Type: String (str1)

Unique values: 2	Missing "": 0/1,201,974
------------------	-------------------------

Tabulation: Freq.	Value
497,292	"A"
704,682	"B"

patid

Patient ID

Type: Numeric (float)

Range: [1,40336]	Units: 1
Unique values: 30,925	Missing .: 0/1,201,974

Mean: 22012  
Std. dev.: 11502.1

Percentiles:	10%	25%	50%	75%	90%
	4905	12317	23294	31822	36940

patid_fl	tag(patid)	
<hr/>		
Type: Numeric (byte)		
Range: [0,1]		Units: 1
Unique values: 2		Missing .: 0/1,201,974
Tabulation: Freq. Value		
1,171,049		0
30,925		1

## Better visualisation of variables

In [6]: `%%stata`  
`inspect`

age: Age (years)					Number of observations		
					Total	Integers	Nonintegers
		#		Negative	-	-	-
		#		Zero	-	-	-
		#		Positive	1,201,974	710,366	491,608
		#					
	#	#	#	Total	1,201,974	710,366	491,608
	.	#	#	Missing	-		
+-----					-----		
14				100	1,201,974		
(More than 99 unique values)							
gender: Gender					Number of observations		
					Total	Integers	Nonintegers
		#		Negative	-	-	-
		#		Zero	542,654	542,654	-
	#	#		Positive	659,320	659,320	-
	#	#					
	#	#		Total	1,201,974	1,201,974	-
	#	#		Missing	-		
+-----					-----		
0				1	1,201,974		
(2 unique values)							
iculos: ICU length-of-stay (hours since					Number of observations		
					Total	Integers	Nonintegers
	#			Negative	-	-	-
	#			Zero	-	-	-
	#			Positive	1,201,974	1,201,974	-
	#						
	#			Total	1,201,974	1,201,974	-
	#	.	.	Missing	-		
+-----					-----		
1				336	1,201,974		
(More than 99 unique values)							
hr: Heart rate (beats per minute)					Number of observations		
					Total	Integers	Nonintegers
	#			Negative	-	-	-
	#			Zero	-	-	-
	#			Positive	1,070,807	1,007,942	62,865
	#						
	#			Total	1,070,807	1,007,942	62,865
	.	#	#	Missing	131,167		
+-----					-----		
20				223	1,201,974		
(More than 99 unique values)							
temp: Temperature (Deg C)					Number of observations		
					Total	Integers	Nonintegers
		#		Negative	-	-	-
		#		Zero	-	-	-
		#		Positive	379,653	38,069	341,584
		#					
		#		Total	379,653	38,069	341,584
	.	.	#	Missing	822,321		
+-----					-----		
20.9				50	1,201,974		

(More than 99 unique values)

sbp: Systolic BP (mm Hg)

Number of observations

					Total	Integers	Nonintegers
	#			Negative	-	-	-
	#			Zero	-	-	-
	#			Positive	1,025,227	958,406	66,821
	#	#					
	#	#		Total	1,025,227	958,406	66,821
	.	#	#	Missing	176,747		
20				298	1,201,974		

(More than 99 unique values)

dbp: Diastolic BP (mm Hg)

Number of observations

					Total	Integers	Nonintegers
	#			Negative	-	-	-
	#			Zero	-	-	-
	#			Positive	828,796	778,982	49,814
	#	#					
	#	#		Total	828,796	778,982	49,814
	#	#	.	Missing	373,178		
20				300	1,201,974		

(More than 99 unique values)

resp: Respiration rate (breaths per min

Number of observations

					Total	Integers	Nonintegers
	#			Negative	-	-	-
	#			Zero	-	-	-
	#			Positive	996,932	940,490	56,442
	#	#					
	#	#		Total	996,932	940,490	56,442
	#	#	.	Missing	205,042		
1				100	1,201,974		

(More than 99 unique values)

o2sat: Pulse oximetry (%)

Number of observations

					Total	Integers	Nonintegers
		#		Negative	-	-	-
		#		Zero	-	-	-
		#		Positive	1,031,430	971,400	60,030
		#					
		#		Total	1,031,430	971,400	60,030
	.	.	.	Missing	170,544		
20				100	1,201,974		

(More than 99 unique values)

map: Mean arterial pressure (mm Hg)

Number of observations

					Total	Integers	Nonintegers
	#			Negative	-	-	-
	#			Zero	-	-	-
	#			Positive	1,038,622	894,718	143,904
	#	#					
	#	#		Total	1,038,622	894,718	143,904
	#	#	.	Missing	163,352		



```

+-----+-----+
20              300              1,201,974
(More than 99 unique values)

sepsislabel:  SepsisLabel
+-----+-----+-----+
#              Negative      Total      Integers      Nonintegers
#              Zero          1,200,317    1,200,317          -
#              Positive      1,657      1,657          -
#              Total          1,201,974    1,201,974          -
#              Missing        -
+-----+-----+-----+
0              1              1,201,974
(2 unique values)

hospid:  Hospital ID
+-----+-----+-----+
#              Negative      Total      Integers      Nonintegers
#              Zero          -          -          -
#              Positive      -          -          -
#              Total          -          -          -
#              Missing      1,201,974
+-----+-----+-----+
.              -9.0e+307      1,201,974
(0 unique value)

patid:  Patient ID
+-----+-----+-----+
#              Negative      Total      Integers      Nonintegers
#              Zero          -          -          -
#              Positive      1,201,974    1,201,974          -
#              Total          1,201,974    1,201,974          -
#              Missing        -
+-----+-----+-----+
1              40336          1,201,974
(More than 99 unique values)

patid_fl:  tag(patid)
+-----+-----+-----+
#              Negative      Total      Integers      Nonintegers
#              Zero          1,171,049    1,171,049          -
#              Positive      30,925      30,925          -
#              Total          1,201,974    1,201,974          -
#              Missing        -
+-----+-----+-----+
0              1              1,201,974
(2 unique values)

```

## Complete case indicator

```

In [7]: %%stata
egen nvar_miss = rowmiss(o2sat hr temp sbp map resp)
gen cc_fl = (nvar_miss == 0)

```

```
. egen nvar_miss = rowmiss(o2sat hr tempsbp map resp)

. gen cc_fl = (nvar_miss == 0)

.
```

In [8]: `%%stata`  
`tab cc_fl`

cc_fl	Freq.	Percent	Cum.
0	865,835	72.03	72.03
1	336,139	27.97	100.00
Total	1,201,974	100.00	

Only 28% of records have no missing vital signs

## Outcome exploration

How many people were diagnosed with sepsis?

In [9]: `%%stata`  
`tab sepsislabel`

SepsisLabel	Freq.	Percent	Cum.
0	1,200,317	99.86	99.86
1	1,657	0.14	100.00
Total	1,201,974	100.00	

When do people get sepsis in ICU?

In [10]: `%%stata`

```
gen time_to_sepsis_temp = iculos if sepsislabel == 1
egen time_to_sepsis = min(time_to_sepsis_temp), by(patid)

. gen time_to_sepsis_temp = iculos if sepsislabel == 1
(1,200,317 missing values generated)

. egen time_to_sepsis = min(time_to_sepsis_temp), by(patid)
(1,093,032 missing values generated)

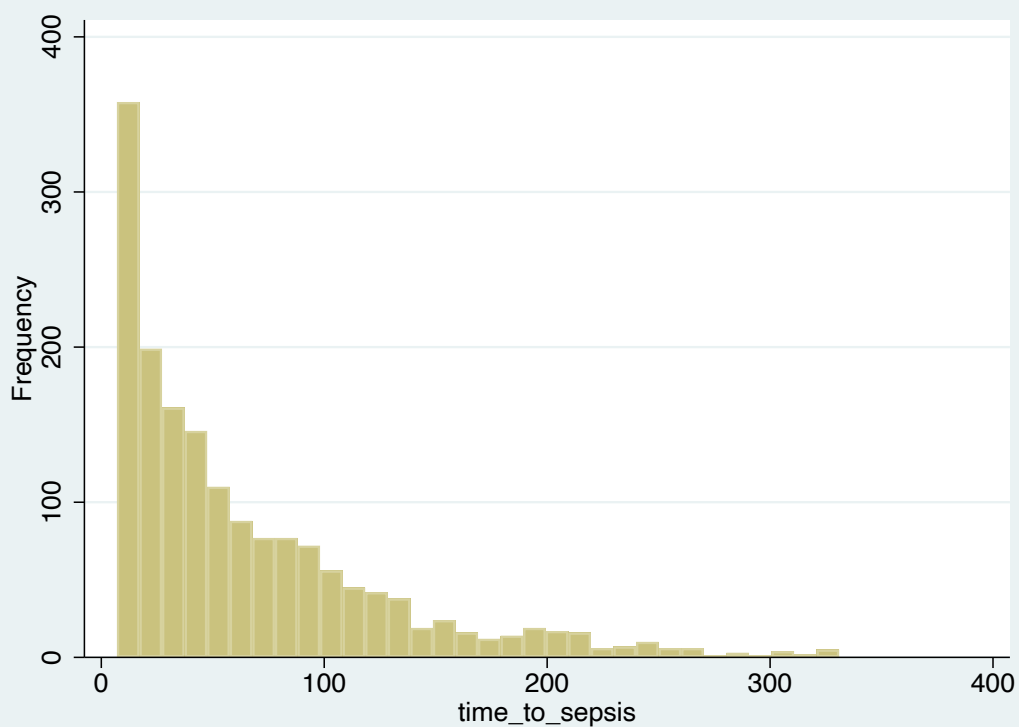
.
```

In [11]: `%%stata`  
`su time_to_sepsis if patid_fl == 1, d`

time_to_sepsis				
-----				
	Percentiles	Smallest		
1%	7	7		
5%	9	7		
10%	11	7	Obs	1,657
25%	20	7	Sum of wgt.	1,657
50%	45		Mean	65.74653
		Largest	Std. dev.	60.86024
75%	91	325		
90%	152	327	Variance	3703.968
95%	200	331	Skewness	1.598774
99%	267	331	Kurtosis	5.555945

- min: 7 hours
- max: 331 hours (13.8 days)
- median: 45 hours

```
In [12]: %%stata
hist time_to_sepsis if patid_f1 == 1, frequency bin(32) start(7)
(bin=32, start=7, width=10.125)
```



Create indicator for patient who get sepsis:

```
In [13]: %%stata
egen any_sepsis = max(sepsislabel), by(patid)
```

Drop ICULOS  $\geq 6$

```
In [14]: %%stata
drop if iculos >= 6
```

(1,047,349 observations deleted)

# Imputing explanatory measures

## Mean Imputation

```
In [15]: %%stata
foreach var of varlist o2sat hr temp sbp dbp map resp {

egen `var' _mean = mean(`var') if iculos <= 5, by(patid)
gen `var' _imp1 = `var'
replace `var' _imp1 = `var' _mean if `var' _imp1 ==. & iculos <= 5

}

. foreach var of varlist o2sat hr temp sbp dbp map resp {
2.
. egen `var' _mean = mean(`var') if iculos <= 5, by(patid)
3. gen `var' _imp1 = `var'
4. replace `var' _imp1 = `var' _mean if `var' _imp1 ==. & iculos <= 5
5.
. }
(2,065 missing values generated)
(41,765 missing values generated)
(39,700 real changes made)
(1,310 missing values generated)
(39,034 missing values generated)
(37,724 real changes made)
(27,860 missing values generated)
(113,581 missing values generated)
(85,721 real changes made)
(4,055 missing values generated)
(42,929 missing values generated)
(38,874 real changes made)
(34,855 missing values generated)
(67,216 missing values generated)
(32,361 real changes made)
(3,170 missing values generated)
(41,707 missing values generated)
(38,537 real changes made)
(5,140 missing values generated)
(47,247 missing values generated)
(42,107 real changes made)
.
```

## First observation carried backwards

```
In [16]: %%stata
foreach var of varlist o2sat hr temp sbp dbp map resp {

gen `var' _imp2 = `var'
by patid (iculos), sort: replace `var' _imp2 = `var' [_n+1] if `var' == .
by patid (iculos), sort: replace `var' _imp2 = `var' [_n+2] if `var' == . & `var' [_n+1] == .
by patid (iculos), sort: replace `var' _imp2 = `var' [_n+3] if `var' == . & `var' [_n+1] == . & `var' [_n+2] == .

}
```

```

by patid (iculos), sort: replace `var'_imp2 = `var'[_n+4] if `var' == . & `var'[_n+1]
== . & `var'[_n+2] == . & `var'[_n+3] == .
}

. foreach var of varlist o2sat hr temp sbp dbp map resp {
2.
. gen `var'_imp2 = `var'
3. by patid (iculos), sort: replace `var'_imp2 = `var'[_n+1] if `var' == .
4. by patid (iculos), sort: replace `var'_imp2 = `var'[_n+2] if `var' == . &
> `var'[_n+1] == .
5. by patid (iculos), sort: replace `var'_imp2 = `var'[_n+3] if `var' == . &
> `var'[_n+1] == . & `var'[_n+2] == .
6. by patid (iculos), sort: replace `var'_imp2 = `var'[_n+4] if `var' == . &
> `var'[_n+1] == . & `var'[_n+2] == . & `var'[_n+3] == .
7. }
(41,765 missing values generated)
(32764 real changes made)
(2296 real changes made)
(773 real changes made)
(301 real changes made)
(39,034 missing values generated)
(32558 real changes made)
(1700 real changes made)
(545 real changes made)
(226 real changes made)
(113,581 missing values generated)
(27896 real changes made)
(16913 real changes made)
(10468 real changes made)
(4976 real changes made)
(42,929 missing values generated)
(32398 real changes made)
(2237 real changes made)
(706 real changes made)
(281 real changes made)
(67,216 missing values generated)
(25592 real changes made)
(2307 real changes made)
(916 real changes made)
(385 real changes made)
(41,707 missing values generated)
(32667 real changes made)
(2054 real changes made)
(540 real changes made)
(204 real changes made)
(47,247 missing values generated)
(32729 real changes made)
(3169 real changes made)
(1119 real changes made)
(441 real changes made)
.

```

## Inspect missingness again among imputed variables

```

In [17]: %%stata
egen nvar_miss_imp1 = rowmiss(o2sat_imp1 hr_imp1 temp_imp1 sbp_imp1 map_imp1
resp_imp1)
gen cc_fl_imp1 = (nvar_miss_imp1 == 0)

```

```
. egen nvar_miss_imp1 = rowmiss(o2sat_imp1 hr_imp1 temp_imp1 sbp_imp1 map_imp1
> resp_imp1)

. gen cc_fl_imp1 = (nvar_miss_imp1 == 0)

.
```

```
In [18]: %%stata
tab cc_fl_imp1 if iculos == 1
```

cc_fl_imp1	Freq.	Percent	Cum.
0	6,897	22.30	22.30
1	24,028	77.70	100.00
Total	30,925	100.00	

```
In [19]: %%stata
egen nvar_miss_imp2 = rowmiss(o2sat_imp2 hr_imp2 temp_imp2 sbp_imp2 map_imp2
resp_imp2)
gen cc_fl_imp2 = (nvar_miss_imp2 == 0)

. egen nvar_miss_imp2 = rowmiss(o2sat_imp2 hr_imp2 temp_imp2 sbp_imp2 map_imp2
> resp_imp2)

. gen cc_fl_imp2 = (nvar_miss_imp2 == 0)

.
```

```
In [20]: %%stata
tab cc_fl_imp2 if iculos == 1
```

cc_fl_imp2	Freq.	Percent	Cum.
0	6,897	22.30	22.30
1	24,028	77.70	100.00
Total	30,925	100.00	

78% of rows non-missing for each imputation method

## Modelling

### Dummy indicators for hospital:

```
In [21]: %%stata
qui ta hospid, gen(h_)
```

can use these to include hospital as a fixed-effect (i.e. create intercepts specific each hospital) We cannot include hospital as a random-effect as there are too few hospitals ( $n = 2$ )

### Mean imputation

```
In [22]: %%stata
glm any_sepsis age i.gender o2sat_imp1 hr_imp1 temp_imp1 ///
```

```

sbp_imp1 map_imp1 resp_imp1 h_* if iculos == 1, ///
    f(binomial) l(logit) eform nocons

. glm any_sepsis age i.gender o2sat_imp1 hr_imp1 temp_imp1 ///
>     sbp_imp1 map_imp1 resp_imp1 h_* if iculos == 1, ///
>     f(binomial) l(logit) eform nocons

Iteration 0:    log likelihood = -5153.728
Iteration 1:    log likelihood = -4666.1855
Iteration 2:    log likelihood = -4660.7151
Iteration 3:    log likelihood = -4660.7019
Iteration 4:    log likelihood = -4660.7019

Generalized linear models                               Number of obs   =    24,028
Optimization      : ML                               Residual df     =    24,018
                                                         Scale parameter =         1
Deviance          =  9321.403872                       (1/df) Deviance =   .3881008
Pearson           =  24067.04487                       (1/df) Pearson  =   1.002042

Variance function: V(u) = u*(1-u)                     [Bernoulli]
Link function     : g(u) = ln(u/(1-u))                 [Logit]

Log likelihood    = -4660.701936                       AIC              =   .3887716
                                                         BIC              =  -232947.6

-----
| any_sepsis | | OIM |
|             | | Odds ratio | std. err. | z | P>|z| | [95% conf. interval] |
|-----|
| age | | 1.001539 | .0018761 | 0.82 | 0.412 | .9978689 | 1.005223 |
| 1.gender | | 1.199998 | .072528 | 3.02 | 0.003 | 1.065942 | 1.350912 |
| o2sat_imp1 | | 1.014293 | .0116994 | 1.23 | 0.219 | .99162 | 1.037485 |
| hr_imp1 | | 1.011688 | .001856 | 6.33 | 0.000 | 1.008057 | 1.015332 |
| temp_imp1 | | 1.007845 | .0409001 | 0.19 | 0.847 | .9307876 | 1.091282 |
| sbp_imp1 | | 1.002924 | .0025617 | 1.14 | 0.253 | .9979156 | 1.007957 |
| map_imp1 | | .9834032 | .0037638 | -4.37 | 0.000 | .976054 | .9908078 |
| resp_imp1 | | 1.051651 | .0066237 | 8.00 | 0.000 | 1.038748 | 1.064713 |
| h_1 | | .0041008 | .0077053 | -2.93 | 0.003 | .0001032 | .1630202 |
| h_2 | | .0026748 | .0050206 | -3.16 | 0.002 | .0000675 | .1059197 |
|-----|
.

```

## First observation carried backwards

```

In [23]: %%stata
glm any_sepsis age i.gender o2sat_imp2 hr_imp2 temp_imp2 ///
    sbp_imp2 map_imp2 resp_imp2 h_* if iculos == 1, ///
    f(binomial) l(logit) eform nocons

```

```
. glm any_sepsis age i.gender o2sat_imp2 hr_imp2 temp_imp2 ///
>      sbp_imp2 map_imp2 resp_imp2 h_* if iculos == 1, ///
>      f(binomial) l(logit) eform nocons
```

```
Iteration 0:    log likelihood = -5157.6504
Iteration 1:    log likelihood = -4675.2941
Iteration 2:    log likelihood = -4669.9801
Iteration 3:    log likelihood = -4669.968
Iteration 4:    log likelihood = -4669.968
```

```
Generalized linear models              Number of obs   =    24,028
Optimization      : ML                 Residual df     =    24,018
                                      Scale parameter =         1
Deviance          =  9339.936077        (1/df) Deviance =   .3888723
Pearson           =  23968.24797        (1/df) Pearson  =   .9979286
```

```
Variance function: V(u) = u*(1-u)      [Bernoulli]
Link function      : g(u) = ln(u/(1-u)) [Logit]
```

```
Log likelihood    = -4669.968038        AIC              =   .3895429
                                      BIC              =  -232929
```

any_sepsis	Odds ratio	OIM std. err.	z	P> z	[95% conf. interval]	
age	1.002013	.0018614	1.08	0.279	.9983715	1.005668
1.gender	1.196948	.072237	2.98	0.003	1.063419	1.347243
o2sat_imp2	.9965014	.0086822	-0.40	0.687	.979629	1.013664
hr_imp2	1.011157	.0016878	6.65	0.000	1.007855	1.014471
temp_imp2	1.037102	.0396564	0.95	0.341	.9622185	1.117814
sbp_imp2	1.001067	.0021664	0.49	0.622	.9968301	1.005322
map_imp2	.987956	.0031389	-3.81	0.000	.9818231	.9941272
resp_imp2	1.034666	.0053817	6.55	0.000	1.024171	1.045267
h_1	.0097567	.0161203	-2.80	0.005	.0003828	.2487049
h_2	.0062195	.0102539	-3.08	0.002	.0002457	.1574373

## Higher respiration rate among those with sepsis?

```
In [24]: %%stata
bysort any_sepsis: su resp_imp1 if patid_fl == 1
```

```
-> any_sepsis = 0
```

Variable	Obs	Mean	Std. dev.	Min	Max
resp_imp1	28,308	18.18708	4.422866	1	98

```
-> any_sepsis = 1
```

Variable	Obs	Mean	Std. dev.	Min	Max
resp_imp1	1,589	19.58373	5.544236	1	44.5

```
In [25]: %%stata
```



```
bysort any_sepsis: su resp_imp2 if patid_fl == 1
```

```
-> any_sepsis = 0
```

Variable	Obs	Mean	Std. dev.	Min	Max
resp_imp2	28,308	18.17834	5.196284	1	98

```
-> any_sepsis = 1
```

Variable	Obs	Mean	Std. dev.	Min	Max
resp_imp2	1,589	19.54751	6.075533	1	50