

November 14, 2017-August 2018
Data known and updates of follow-up

Here, we bring in the Dataset and update the Date of Last Follow-up column. Then, we remove SCLC (Small Cell Lung CA) patients since we're interested in the ADC (Adenocarcinoma) patients.

The DR lock date was the date this analysis was started: 07/26/17. No new patients since 07/26/17 are included in this analysis. However, the most updated follow-up data was merged to the dataset as of 12/29/17, so we have 8 month follow-up data ahead for all patients. For follow-up, we left join the database with the most recent follow-up data ([FollowUpJoinDB](#), [ManualJoinDB](#)). This is done to make sure that the DeathLast Follow-up, [updateLastFollowUpData.sql](#), [get_data.py](#), [most_recent_update_db.py](#), [merge.py](#), [updateLastFollowUpData.py](#).

Summary Statistics

The data is still pretty messy at this point. The column headings are cumbersome, and the factor levels for things like sex are not fixed (for instance, see lists M, W and F as factors - this needs to be trimmed back to just M and F). We are first just doing some poking around the raw data and generating some "Table 1"-type numbers. We will fix the column headings and shape up the data later prior to modeling.

Race	x
A	5
B	7
C	1
D	30

```
approximateProportion(1:4*Pr(Race, fac1=as.factor(broomeromies$Pr(Race)), #Broomeromies$
```

Race	x
A	3
B	20
C	1
D	1
E	1
F	192

```
# test for significant difference in age between groups
t.test(Promoter1$age, Nonpromoter1$age)

##
## Welch Two-Sample t-test
##
## data: Promoter1$age and Nonpromoter1$age
## t = 0.58888, df = 68.418, p-value = 0.5507
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
## -1.420176 1.487487
## sample estimates:
## mean of x mean of y
## 70.31000 68.90184

# note: t-tests for promotoric patients, patients without promotoric and all patients, respectively
exp.test(Promoter1$cellType, Nonpromoter1$cellType) # F(5,61)=0.68
```

Sex	x
F	18
M	21

```
aggregate (iris$sepal.length ~ iris$sex, iris, list (function(x) sum(x), FUN=length))
```

Sex	n
F	73
M	1
NA	92

```
summary(wFIS, aFDname, kplot=(sum(wFIS, aFDname), FIS(is.na(wFIS)))
```

Sex	n
F	91
M	5
NA	113

Smoking Status	x
Current	2
Former	31
Never	6

Smoking Status	x
Current	13
Former	120
Never	23

Smoking Status	x
Current	15
Former	151
Never	39

```

# Cancer Histology
# Cancer Histology in patients with PD-L1 immunohistochemistry
aggregate(Pancreas14Data$HISTOL, by=c("HISTOL", "HISTOL$Immunohistochemistry"), FUN=length)

```

MBLCL Histology	n
Adenocarcinoma	18
Large cell neuroendocrine carcinoma	3
Mesothelioma	1
Poorly differentiated carcinoma	1
Squamous cell carcinoma	16

NBOLC Histology	%
Adenocarcinoma	55
Adenosquamous carcinoma	1
Squamous carcinoma	1
Carcinoma	1
Large cell neuroendocrine carcinoma	1
Mesothelioma	1
Poorly differentiated carcinoma	1
Sarcomatoid carcinoma	1
Squamous cell carcinoma	1

NSCLC Histology	
Adenocarcinoma	13%
Adenosquamous carcinoma	1%
Squamous carcinoma	1%
Carcinoma	1%
Large cell neuroendocrine carcinoma	1%
Mesothelioma	1%
Poorly-differentiated carcinoma	1%
Sarcomatoid carcinoma	1%
Squamous cell carcinoma	1%

```
# Cancer Stage
# Cancer stage is patients with PD-1 germline
aggregate(Presumptions[Initial.Cancer.Stage..I..II..III..IV..], bylist(Initial.Cancer.Stage..I..II..III..IV, $Presumptions[Initial.Cancer.Stage..I..II..III..IV..], FUN=length)
```

Initial Cancer Stage: I, II, III, IV	x
I	1
II	5
III	13
IV	19

```
# Cancer History in patients without HIV-1 pneumonia
approximateHIVPneumoniaPwInitial.Cancer.Stage.1..12...29, byInitial.Cancer.Stage.1..12...29, n
approximateHIVPneumoniaPwInitial.Cancer.Stage.1..12...29, HIVLength
```

Initial Cancer Stage: I, II, III, IV	x
I	3
II	16
III	1
IV	12
VI	44
IV	90

```
# Cancer Histology Status is all patients
aggregate(PG_6[Initial.Cancer.Stage..I..III..IV..], bylist(Initial.Cancer.Stage..I..III..IV, PG_6[Initial.Cancer.Stage..I..III..IV], FUN=length)
```

Initial Cancer Stage I, II, III, IV	%
I	17
II	19
III	50
IV	10

P = Parametric Grade breakdown appropriate; Parametric is 1 at 6.82% vs nonparametric Grade(1), P(Binomial) = .000.

```
# Pericarditis Grade breakdown in PD-2 patients
aggregate(Pericarditis[a]~Highest.Pericarditis.Grade, bylist(Highest.Pericarditis.Grade, Pericarditis.Grade), FUN=length)
```

Highest Pneumonia Grade	n
2	54
3	17
4	2
5	0
Unknown	1

```

# prior chemotherapy
aggregate(Presence[inPd]@name, for, initial.treatment, 1, per, 0, na.rm = TRUE)
aggregate(Presence[inPd]@name, for, initial.treatment, 1, per, 1, na.rm = TRUE)
aggregate(Presence[inPd]@name, for, initial.treatment, 1, per, 2, na.rm = TRUE)

```

Chemicals for initial treatment, 1 gms.

```
aggregate(hisParametricPftChans, for, initial, treatment...), par, 0, no., bycolls(chans, for, initial, treatment...), par, 0, no., ncolls(hisParametricPftChans, for, initial, treatment...), par, 0, no., ) %>% fill(nlength)
```

Chemo for initial treatment, % yes...

```
aggregate(FU ~ all(Shmo.for.initial.treatment, 1.yes, 0.no), bylist(Shmo.for.initial.treatment, 1.yes, 0.no, nFU ~ all(Shmo.for.initial.treatment, 1.yes, 0.no)), FUN=length)
```

Chemotherapy treatment, 1.yes

Surgery for initial treatment: Yes

```
aggregate(SoProtonicPallSurgery,for,initial.treatment...1.yes..0.no., bylist(Surgery,for,initial.treatment...1.yes..0.no.,SoProtonicPallSurgery,for,initial.treatment...1.yes..0.no.), FUN=expb)
```

Surgery for initial treatment... Yes...

```
aggregate(PG1_4[!surgery, for, initial.treatment..1.yes..0.no., bylist(surgery, for, initial.treatment..1.yes..0.no.)
+PG1_4[!surgery, for, initial.treatment..1.yes..0.no.), FUN=length)
```

Surgery for initial treatment...yes

48 (2) 39

[illegible]

Pneumonia Outcome: 1. OR Improved; 3. Worsened; actual values are: 1. Completely Resolved; 2. Improved; 4. Stable/Unchanged; 5. Worsened; 6. Unknown	n
1	1
2	1
3	2
4	20
5	0
6	4
Worsened	0

```

# type of immunotherapy for pts with pneumococcal
# aggregate (PneumocilliaPnAFirst, DO, treatment, .Primary, Immunotherapy, Agent, AgeList (First, DO, treatment, .Primary, Im-
# munotherapy, Agent+PneumocilliaPnAFirst, DO, treatment, .Primary, Immunotherapy, Agent), FID=length)

```

First IO treatment_Primary Immunotherapy Agent	n
MSD4736 10-mg/kg Q2 weeks	1
Nivolumab	36
Pembrolizumab	2

```

# type of immunotherapy type for patients without pneumonia
aggregate(HbPercent~1|1$PnEffFirst, Hb, treatment..Primary, Immunotherapy..Agent,
  Kylicik(First, Hb, treatment..Primary, Immunotherapy..Agent|HbPercent~1|1$PnEffFirst, Hb, treatment..Primary, Immunotherapy..Agent), FUN=length)

```

First/20 treatment, Primary Immunotherapy Agent	n
BMS-936559 (MDC-150)	7
Durvalumab	6
MDC1736 20-mg/4 Q4 weeks	4
MDC1736 20-mg/4 Q4 weeks	2
Nivolumab	126
PD03321	2
Pembrolizumab	21
Switch maintenance nivolumab	2

```

A type of immunotherapy for all patients
aggregate(PID, diffFirst, 10, treatment, .Primary, Immunotherapy, Agent, .Hydrex (First, 10, treatment, .Primary, Immunotherapy, Agent) diffFirst, 10, treatment, .Primary, Immunotherapy, Agent), PID (length))

```

First SO treatment, Primary immunotherapy Agent	n
1	1
IMiD-90509 (IMiD-1105)	7
Durvalumab	4
MGD4726 10-mg/kg Q2 weeks	5
MGD4726 20-mg/kg Q4 weeks	2
Nivolumab	160
PD0301	2
Pembrolizumab	23
Switch maintenance nivolumab	

```
# Use of combination therapy
# make therapy for pemmetria pts.
ConstructFromCriteria c" aggregate(PneumoniaFirst.DD.treatment ->Secondary-Agent,
Secondary-Agent-PneumoniaFirst.DD.treatment ->Secondary-Agent),PillLength)
ConstructFromCriteria
```

First-Line Treatment	Secondary Agent	n
Anti-LA22		233
Kazicidine + OC484 + Etravirine (sequential)		1
Kazicidine + Etravirine (sequential)		46
Caripiprin + Picitaxel		1
Cipiprin + Gemcitabine		1
Interferon		

1	Describe the data
2	What is the data type of the variable 'Age'?
3	What is the data type of the variable 'Sex'?
4	What is the data type of the variable 'Status'?
5	What is the data type of the variable 'Age'?
6	What is the data type of the variable 'Sex'?
7	What is the data type of the variable 'Status'?
8	What is the data type of the variable 'Age'?
9	What is the data type of the variable 'Sex'?
10	What is the data type of the variable 'Status'?

Variable	Frequency
Age	100
Sex	100
Status	100
Age	100
Sex	100
Status	100
Age	100
Sex	100
Status	100
Age	100
Sex	100
Status	100

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Variable	Frequency
Age	100
Sex	100
Status	100
Age	100
Sex	100
Status	100
Age	100
Sex	100
Status	100
Age	100
Sex	100
Status	100

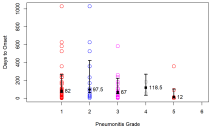
1	Describe the data
2	What is the data type of the variable 'Age'?
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4	What is the data type of the variable 'Status'?
5	What is the data type of the variable 'Age'?
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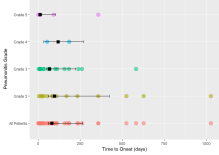
Time to Onset Analysis

This is a log-rank test for time to onset analysis. (Hosmer et al. 2011) for other R packages.

1	Describe the data
2	What is the data type of the variable 'Age'?
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8	What is the data type of the variable 'Age'?
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10	What is the data type of the variable 'Status'?

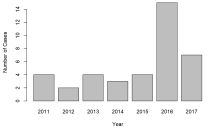


1	Describe the data
2	What is the data type of the variable 'Age'?
3	What is the data type of the variable 'Sex'?
4	What is the data type of the variable 'Status'?
5	What is the data type of the variable 'Age'?
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7	What is the data type of the variable 'Status'?
8	What is the data type of the variable 'Age'?
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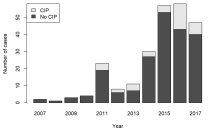
Pneumonia Incidence by Year

Use of Anti-PCP20-1 is not uniform across the 5 years that this data was collected. This analysis looks at incidence by year.

1	Describe the data
2	What is the data type of the variable 'Age'?
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7	What is the data type of the variable 'Status'?
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10	What is the data type of the variable 'Status'?



Modeling: Cox PH and Logistic Regression Models

Now the need of the model. We want to look at all the differences between patients with and without pneumonia using logistic regression (logistic regression) and evaluate the fit of the model. For the Cox PH model, we want to look at the fit of the model. The model is fit using the Cox PH model.

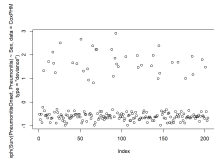
1. Data cleanup for Cox PH Regression analysis

1	Describe the data
2	What is the data type of the variable 'Age'?
3	What is the data type of the variable 'Sex'?
4	What is the data type of the variable 'Status'?
5	What is the data type of the variable 'Age'?
6	What is the data type of the variable 'Sex'?
7	What is the data type of the variable 'Status'?
8	What is the data type of the variable 'Age'?
9	What is the data type of the variable 'Sex'?
10	What is the data type of the variable 'Status'?

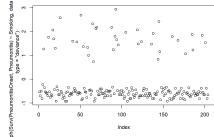
Variable	Frequency
Age	100
Sex	100
Status	100

Figure 1 displays four Kaplan-Meier survival plots showing cumulative survival over time (0 to 1800 days) for different patient groups. The y-axis for all plots is 'Cumulative Survival' ranging from 0.0 to 1.0.

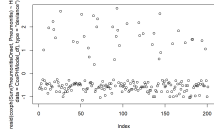
- Top-left plot:** Stratified by Stage (I, II, III, IV). The log rank p-value is 0.0001. Survival increases with stage, with Stage I having the highest survival and Stage IV the lowest.
- Top-right plot:** Stratified by Sex (Male, Female). Survival is generally higher for females than for males across the time period.
- Bottom-left plot:** Stratified by Age (≤ 60, > 60). Survival is generally higher for patients aged ≤ 60 compared to those aged > 60.
- Bottom-right plot:** Stratified by Race (Asian, Black, White, Other). Survival is generally higher for Asian patients compared to other racial groups.



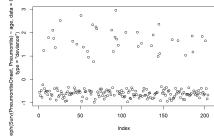
```
plot(randid[rough][SurvParametricOvar, Parametric]) ~ lmering, data=covModel_df, type="deviance")
```



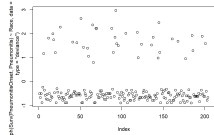
```
plot(ranef(coup[fix(ParametricIntercept, Parametric)]) ~ Weeklog, data=couModel_df, type="deviance")
```



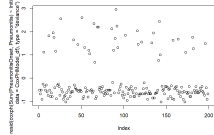
```
plot(covd(covph[Surv(PneumonitisIstest, Pneumonitis)] ~ age, data=linPhModel_df), type="deviance")
```



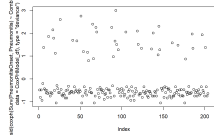
```
plot(nasid(rough(fitParametricOneway, ParametricOneway) ~ Name, dataConfoundModel_did), type="deviance")
```



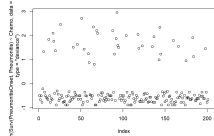
```
plot(namid(cough)~Surv(ParameterEstimate, ParameterEstimate) ~ InitialStage, data=CoughModel_dE, type="n")
```



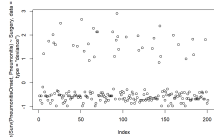
```
plot(ranid(cough(farr(PneumoniaInvert, Pneumonia) ~ Combination_UU, data=couP00del_01), vtype="dev
```



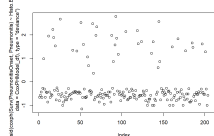
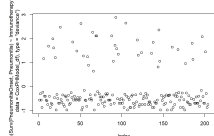
```
plot(rmsd(cough[Surv(PneumoniaInfluenza, Pneumonia)] ~ Chemo, data=couPModel_df), type="deviance")
```



```
plot(rasid(rough(fserv(PneumoniaOnset, Pneumonia)), Burger2, data=Cou798model_4f), type="deviance")
```



```
plot(mold(morph(Surv(PneumoniaOnset, Pneumonia) ~ Immunotherapy_Drug_Record, data=CoxP060del_dfl),
```



```

#end group (set (elementary) elementary) (set (mean (elementary_mean)))

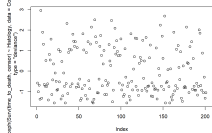
## Cells
## length(Estim = Surv(SymmetricSurv, SymmetricSurv) ~ Sex, data = CoEfficients)
##
## no 250, number of events 38
##
## read exp(misc) misc(misc) ~ Re(misc)
##
## hsc(misc) 0.1987 1.2211 0.3216 0.453 0.34
##
## exp(misc) exp(misc) lower 0.0 upper 0.0
##
## hsc(misc) 1.221 0.319 0.453 0.252 2.312
##
## Coefficient: 0.325 (se = 0.04)
## Coefficient: 0.252 (se = 0.038)
## Substochastic: 0.37 (se = 0.04)
## Substochastic: 0.38 (se = 0.04)
## Coefficient: 0.38 (se = 0.04)
## Coefficient: 0.38 (se = 0.04)

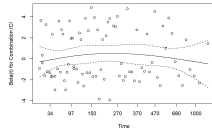
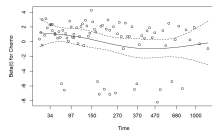
```

```
summary(jgraph(Surv(Parameter1)~death, Parameter1) ~ Smoking, data =
data)

## Call:
## data ~ Surv(Parameter1)~death, Parameter1 ~ Smoking,
## data = CoxModel_fit
##
##  = 204, number of events = 38
##
##      coef(coef) sd(coef) z Pr(>|z|)
## Smoking 0.1223    1.1297  0.3213  0.36    0.750
##
##      exp(coef) exp(-coef) lower .95 upper .95
## Smoking    1.13    0.8852  0.6219    2.221
```

[illegible]



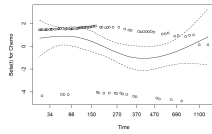


```

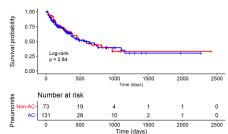
fit <- survfit(surv ~ time, data = fit_data)
plot(fit, main = "Kaplan-Meier Survival Plot")

```

Time	Survival	Lower CI	Upper CI
0	1.000	1.000	1.000
34	0.985	0.975	0.995
97	0.970	0.960	0.980
150	0.955	0.945	0.965
270	0.940	0.930	0.950
370	0.925	0.915	0.935
470	0.910	0.900	0.920
600	0.895	0.885	0.905
1000	0.880	0.870	0.890



NSCLC Survival based on presence of Adenocarcinoma History



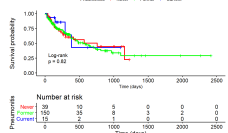
```

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```

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600	0.895	0.885	0.905
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NSCLC Survival based on Smoking Status



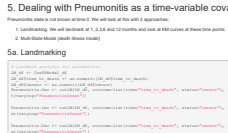
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fit <- survfit(surv ~ time, data = fit_data)
plot(fit, main = "Kaplan-Meier Survival Plot")

```

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600	0.895	0.885	0.905
1000	0.880	0.870	0.890

NSCLC Survival based on presence of pneumonitis starting at 1 month



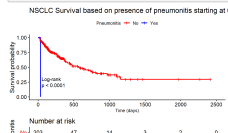
```

fit <- survfit(surv ~ time, data = fit_data)
plot(fit, main = "Kaplan-Meier Survival Plot")

```

Time	Survival	Lower CI	Upper CI
0	1.000	1.000	1.000
34	0.985	0.975	0.995
97	0.970	0.960	0.980
150	0.955	0.945	0.965
270	0.940	0.930	0.950
370	0.925	0.915	0.935
470	0.910	0.900	0.920
600	0.895	0.885	0.905
1000	0.880	0.870	0.890

NSCLC Survival based on presence of pneumonitis at 1 month



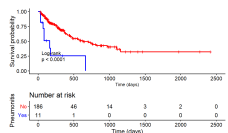
```

fit <- survfit(surv ~ time, data = fit_data)
plot(fit, main = "Kaplan-Meier Survival Plot")

```

Time	Survival	Lower CI	Upper CI
0	1.000	1.000	1.000
34	0.985	0.975	0.995
97	0.970	0.960	0.980
150	0.955	0.945	0.965
270	0.940	0.930	0.950
370	0.925	0.915	0.935
470	0.910	0.900	0.920
600	0.895	0.885	0.905
1000	0.880	0.870	0.890

NSCLC Survival based on presence of pneumonitis at 2 month



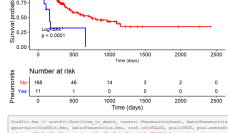
```

fit <- survfit(surv ~ time, data = fit_data)
plot(fit, main = "Kaplan-Meier Survival Plot")

```

Time	Survival	Lower CI	Upper CI
0	1.000	1.000	1.000
34	0.985	0.975	0.995
97	0.970	0.960	0.980
150	0.955	0.945	0.965
270	0.940	0.930	0.950
370	0.925	0.915	0.935
470	0.910	0.900	0.920
600	0.895	0.885	0.905
1000	0.880	0.870	0.890

NSCLC Survival based on presence of pneumonitis at 6 month



```

fit <- survfit(surv ~ time, data = fit_data)
plot(fit, main = "Kaplan-Meier Survival Plot")

```

Time	Survival	Lower CI	Upper CI
0	1.000	1.000	1.000
34	0.985	0.975	0.995
97	0.970	0.960	0.980
150	0.955	0.945	0.965
270	0.940	0.930	0.950
370	0.925	0.915	0.935
470	0.910	0.900	0.920
600	0.895	0.885	0.905
1000	0.880	0.870	0.890

Time (days)	From state 1 (Solid Red)	From state 2 (Dashed Cyan)
0	1.00	1.00
200	0.85	0.75
400	0.70	0.55
600	0.55	0.40
800	0.45	0.25
1000	0.35	0.15

```

graph TD
    S1((State 1)) -- 0.06 --> S2((State 2))
    S2 -- 0.04 --> S1
    S1 -- 0.08 --> S3((State 3))
    S2 -- 0.2 --> S3
    S3 -- 0.74 --> S3
  
```

```

graph TD
    S1((State 1)) -- 0.59 --> S1
    S1 -- 0.13 --> S2((State 2))
    S1 -- 0.32 --> S3((State 3))
    S2 -- 0.87 --> S3
    S3 -- 1.00 --> S3
    style S1 fill:#0000FF,color:#FFFFFF
    style S2 fill:#0000FF,color:#FFFFFF
    style S3 fill:#FF0000,color:#FF0000
  
```

```

graph TD
    S1((State 1)) -- 0.96 --> S1
    S1 -- 0.02 --> S2((State 2))
    S2 -- 1.0 --> S2
    S3((State 3)) -- 0.01 --> S1
    S3 -- 0.09 --> S2

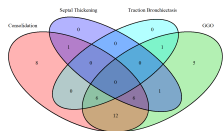
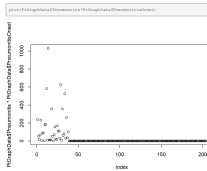
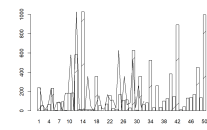
```

```
## Pearson's Chi-squared test with simulated p-value (based on 2000
## replicates)
##
## data: table(cenPHModel$dEfficacy, CenPHModel$dSurgery)
## P-value = 0.79171, df = 14, pvalue = 0.4033
```

```
plot.mcmc(BG.MCMC.ConfHistology, factor(1:2), las=2, nrange=c(0,1000), covariate=list(Histology~"Other"), abline="Time
```


[illegible][illegible][illegible]

Year	No CIP (Black)	CIP (White)	Total
2007	2	0	2
2008	1	0	1
2009	2	0	2
2010	3	0	3
2011	20	3	23
2012	7	2	9
2013	8	3	11
2014	28	3	31
2015	52	5	57
2016	48	8	56
2017	40	8	48

[illegible][illegible]



