PBHS 32100 / STAT 22401 Winter 2024 J. Dignam

Poisson Regression with Incidence Rates

Poisson regression is used to model a non-negative integer **count variables** as the outcome. As mentioned earlier, in Public Health and Epidemiology disease incidence is often studied in relation to exposure over time

- Many deleterious exposures, as well as natural factors such as aging, will have bearing on the event count and must be accounted for when, say, comparing groups.
- Thus, rather than denominator N for a sample, the relevant denominator is the sum of exposure time over all N individuals, known as person-time Rather than proportions, we have rates per unit of time at risk.
- This approach also accommodates different lengths of at risk time that may naturally occur.

Incidence Rates and Ratios

For incidence rate data

- data come in form of events and pyrs, there is no other 'N'. Data may be aggregated already (table form) or listed as individual cases with follow-up time (in which case there will be an 'N'
- latter form is needed for continuous exposure variables

Summary table for an epidemiological study of some exposure

	Exp	osure	Total
	yes	no	
case counts	c_e	c_u	$c_e + c_u = C$
person-years	pyr_e	pyr_u	$pyr_e + pyr_u = PYR$
Incidence rate	$IR_e = c_e/pyr_e$	$IR_u = c_u/pyr_u$	IR = C/PYR

Incidence Rates and Ratios

The following are cardiovascular disease events in relation to two potential risk factors, age group and obesity (y/n). The data (from SPRM Ch 9):

. list, clean noobs

${\tt AgeGroup}$	Obesit~s	cvd	pyrs	${\tt agegrp}$	obstat
60{64	Obese	10	245	1	1
60{64	Notobese	12	640	1	0
65{69	Obese	34	365	2	1
65{69	Notobese	45	520	2	0
70{74	Obese	40	250	3	1
70{74	Notobese	44	490	3	0

If we consider the obesity factor pnly, and sum the data to fill the table, we have

Obesity

	yes	no	Total
CVD cases	84	101	185
person-years	860	1650	2510
Incidence rate	.0976744	.0612121	.0737052

Previously we saw the ratio of count proportions as a natural summary from the Poisson model, showing how counts increase on a multiplicative scale

The incidence rate ratio is defined similarly as

$$\frac{IR_e}{IR_u} = \frac{.0977}{.0612} = 1.5956$$

Indicating about a 1.6 fold excess risk for the obese group

The Incidence Rate Ratio

STATA has modules to perform these types of epidemiologic summaries/analyses functions. The *incidence rate* command:

. ir cvd obstat pyrs

	obstat Exposed	Unexposed	 	Total		
pyrs	84 860	1650	Ì	2510		
Incidence rate			·			
		estimate	-		_	
Inc. rate diff.	.03	864623	Ι.	0124039	.0605207	
Inc. rate ratio	1.5	95671	1	.180226	2.15264	(exact)
Attr. frac. ex.	.37	'33045	1 .	1527047	.535454	(exact)
Attr. frac. pop	.16	395004 	 			

Poisson Regression Model (and other GLMs) - a note on model fitting

- The Poisson model and other GLMs are fit via maximum likelihood estimation. Least squares is an MLE estimator, but only for linear regression
- the Likelihood Function $L=f(Y_1,Y_2,\ldots,Y_n|\omega)$ is a key quantity. It is the joint distribution of all the observations (data fixed), expressed as a function of all the parameters (ω) . The method finds the values of the parameters (including β s) that most likely gave rise to the data. This is done by taking derivatives of $\log(L)$ with respect to parameters, setting equal to zero and solving.
- After the fit, L is a quantity (computed by plugging in those parameters) that can be used to compare models, measure 'fit', etc. We usually work with the log likelihood, provided with every model run.

Poisson Regression Model for Incidence Rates

We can fit the model as in the count case. An important difference is the inclusion of the 'exposure' variable to indicate the person-years

Note: $_cons$ estimates baseline incidence rate.

The non-obese incidence rate and multiplicative effect of obesity (i.e.,

the IRR) are produced.

cvd	IF	R Std. Err	. z	P> z	[95% Conf	. Interval]
obstat _cons ln(pyrs)	.061212		-28.07		1.194671 .0503663	2.13127 .0743935

Note: _cons estimates baseline incidence rate.

Note that .0612 or 6.1/100 person-years is the incidence rate in the non-obese and $..06125 \cdot 1.5956 = .09767$ or 9.8/100 person-years is the rate in the obese group, reproducing the numbers in the earlier table.

Poisson Model for Incidence Rates - add an ordinal predictor

We can add the age group variable as an ordinal predictor. Examine CVD by age:

```
. tabstat cvd pyrs, by(AgeGroup) stat(sum)
Summary statistics: sum by categories of: AgeGroup
```

AgeGroup	1	cvd	pyrs
60{64 65{69 70{74	Ì	22 79 84	885 885 740
Total	+ 	185	2510

. display 22/885

.02485876

. display 79/885

.08926554

. display 84/740

.11351351

Poisson Model for Incidence Rates - add an ordinal predictor

. poisson cvd obstat agegrp, exposure(pyrs) irr

Iteration 0: log likelihood = -21.297411
Iteration 1: log likelihood = -21.297215
Iteration 2: log likelihood = -21.297215

Poisson regression	Number of obs	=	6
	LR chi2(2)	=	53.15
	Prob > chi2	=	0.0000
Log likelihood = -21.297215	Pseudo R2	=	0.5551

cvd		Std. Err.	z	P> z	[95% Conf.	Interval]
obstat agegrp _cons ln(pyrs)	1.535171 1.871195 .0162154	.2267304 .1845068 .0040498 (exposure)	2.90 6.35 -16.50	0.004 0.000 0.000	1.149323 1.542366 .009939	2.050554 2.27013 .0264555

Note: _cons estimates baseline incidence rate.

Model here is on IRR scale

Poisson Model for Incidence Rates - Meaning of Predictor Coefficients

exp(coefficient) yield the relative increase/decrease (i.e the IRR) for change in exposure level

- a. cons = .0162 estimated mean CVD rate for non-obese, agegrp = 1
- b. $\beta_{agegrp}=1.87$ Indicating a 1.87-fold increase in CVD rate per age group increase
- c. $\beta_{obstat}=1.535$ Indicating a 1.54-fold increase in CVD for obese vs. nonobese- similar to earlier

Poisson Regression - Categorical Predictor for Age

. poisson cvd obstat age2 age3, exposure(pyrs) irr

```
Iteration 0: log likelihood = -17.107802
Iteration 1: log likelihood = -17.083109
Iteration 2: log likelihood = -17.083097
Iteration 3: log likelihood = -17.083097
```

Poisson regression	Number of obs	=	6
	LR chi2(3)	=	61.58
	Prob > chi2	=	0.0000
Log likelihood = -17.083097	Pseudo R2	=	0.6432

cvd	IRR	Std. Err.	z	P> z	[95% Conf.	Interval]
obstat	1.468678	.2180134	2.59	0.010	1.097924	1.964629
age2	3.399674	.8229289	5.06	0.000	2.115409	5.463615
age3	4.453633	1.067596	6.23	0.000	2.784004	7.124574
_cons	.0220038	.0048363	-17.36	0.000	.0143025	.0338521
ln(pyrs)	1	(exposure)				

Note: _cons estimates baseline incidence rate.

The CVD data was aggregated by groups (age x obesity) with event counts. We can also work with individual data, where each individual either does or does not have the event over some follow-up time

Ex/ Endometrial cancer among women receiving tamoxifen/placebo in a breast cancer clinical trial. Tamoxifen is associated with increased risk, but is uncommon relative the studied group (N > 2800) and amount of follow-up time:

.. list id trt menstat age bmi endo, clean

		id	trt	me	enstat	age	bmi	endo
371.	635	1		3	67	36.6	0	
372.	640	1		1	35	20.1	0	
373.	642	1		3	50	19.6	0	
374.	644	2		3	65	25.3	1	
375.	646	1		3	58	35.7	0	
376.	649	2		3	59	30.1	0	
	•							

The data summarized via Incidence Rate analysis (*timefree* is the exposure time)

. ir endo trtx timefree Incidence-rate comparison

Incidence-late comparison							
	t:	rtx	1				
	Exposed	Unexposed	Total				
endo	13	3	16	i I			
timefree	90322.5 +	79946.1	170268.6 -+				
Incidence rate	.0001439 	.0000375	.000094	i.			
	Point	estimate	[95% Co	nf. Interval]			
Inc. rate diff.	.00	001064	.000017	4 .0001954			
Inc. rate ratio	3.8	835513	1.05398	9 20.98384	(exact)		
Attr. frac. ex.	1 .73	.7392787		7 .9523443	(exact)		
Attr. frac. pop	.6006639		 				

Use Poisson model:

```
. poisson endo trtx, exposure(timefree)
            log likelihood = -93.429861
Iteration 0:
Iteration 1: log likelihood = -93.428424
Iteration 2: log likelihood = -93.428424
Poisson regression
                                       Number of obs = 1,395
                                                      = 5.58
                                       LR chi2(1)
                                       Prob > chi2 =
                                                           0.0182
Log likelihood = -93.428424
                                       Pseudo R2 =
                                                           0.0290
      endo | Coef. Std. Err. z P>|z| [95% Conf. Interval]
      trtx | 1.344303 .6405126 2.10 0.036 .0889214 2.599685
     _cons | -10.1905 .5773502 -17.65 0.000 -11.32208 -9.05891
ln(timefree) | 1 (exposure)
```

[.] display exp(1.344303)

^{3.8355123}

Poisson approach allows incorporation of covariates:

. poisson endo trtx age bmi, exposure(timefree) ir

Iteration 0: log likelihood = -92.189405
Iteration 1: log likelihood = -92.187682
Iteration 2: log likelihood = -92.187682

Poisson regre	aci,	nn -			Number o	f obs	=	1,395
Poisson regression				Number 0.	1 005	_	1,000	
					LR chi2(3)	=	8.06
					Prob > cl	hi2	=	0.0448
Log likelihoo	od =	-92.18768	2		Pseudo R	2	=	0.0419
endo		IRR	Std. Err.	z	P> z	[95%	Conf.	Interval]
trtx	i	3.715235	2.381092	2.05	0.041	1.057	7917	13.04731
age	1	1.032185	.0297447	1.10	0.272	.975	5024	1.092161
bmi	1	1.040999	.0452663	0.92	0.355	.9559	9539	1.133609
_cons	1	2.23e-06	4.38e-06	-6.62	0.000	4.71	80-e	.0001052
<pre>ln(timefree)</pre>	1	1	(exposure)					

Note: _cons estimates baseline incidence rate.

Poisson Regression - Testing individual Coefficients

We can test the value of individual covariates as in SLR/MLR. We test

$$H_0 : IRR = e^{\beta} = 1$$

which is is same as

$$H_0: \log(IRR) = \beta = 0$$

VS.

$$H_A: \log(IRR) \neq \beta = 0$$

Theory from GLMs and the estimation method shows that β is \approx Normal. The test statistic (reported in the STATA/R output) for the above hypothesis is:

$$Z = \frac{\beta (-0)}{\hat{\operatorname{se}}(\hat{\beta})}$$

Poisson Regression - Testing the Whole Model

When we execute the model, the following summary precedes the

The likelihood ratio test (LR above, equaling 61.58)) is s function of the difference in likelihoods for this model vs. a *null* model with no predictors. This is tantamount to the overall F test in LR.

To illusdtrate, we can run the two models and contrast

- .* RUN null model
- . poisson cvd, exposure(pyrs) irr

Iteration 0: log likelihood = -47.874227
Iteration 1: log likelihood = -47.874227

Poisson regression Number of obs = 6LR chi2(0) = -0.00Prob > chi2 = .

Log likelihood = -47.874227 Pseudo R2 = -0.0000

- . * SAVE it
- . est store nul

.

- .* RUN full model
- . poisson cvd obstat age2 age3, exposure(pyrs) irr

Iteration 0: log likelihood = -17.107802

. . .

Iteration 3: log likelihood = -17.083097

Poisson regression Number of obs = 6LR chi2(3) = 61.58Prob > chi2 = 0.0000

```
Log likelihood = -17.083097

Pseudo R2 = 0.6432

. . .

* SAVE it

est store big

.

* CONTRAST these models

. lrtest big nul

Likelihood-ratio test

(Assumption: nul nested in big)

Pseudo R2 = 0.6432

LR chi2(3) = 61.58
```

The above computation (test statistic is)

$$D = -2\{\log \hat{L_n} - \log \hat{L_b}\}$$

which here is

$$-2\{ -47.874 - (-17.083)\} = 61.58$$

This is compared to a χ^2 statistic with degrees of freedom equal to the number of parameters (3 here). Result is to reject the null hypothesis that the likelihood ratio is 1.

Poisson Regression - Testing Subsets of Parameters

Contrasting different models follows the same strategy - contrasting the likelihood values between models.

- For example, to test the contribution of the categorical age variable (2 indicators), we can run the two models and compute as above.
- Alternatively, we can use a post-estimation test as done earlier in SLR/MLR. This is a different test (Wald test) but inference should be similar to LR test.

Poisson Regression - Testing Subsets of Parameters

```
. poisson cvd obstat age2 age3, exposure(pyrs) irr
Iteration 3: log likelihood = -17.083097
Poisson regression
                                       Number of obs =
                                       LR chi2(3)
                                                           61.58
                                       Prob > chi2
                                                          0.0000
Log likelihood = -17.083097
                                      Pseudo R2
                                                          0.6432
       cvd | IRR Std. Err. z P>|z| [95% Conf. Interval]
    obstat | 1.468678 .2180134 2.59 0.010 1.097924 1.964629
      age2 | 3.399674 .8229289 5.06 0.000 2.115409 5.463615
      age3 | 4.453633 1.067596 6.23 0.000 2.784004 7.124574
     _cons | .0220038 .0048363 -17.36 0.000 .0143025
                                                        .0338521
   ln(pyrs) | 1 (exposure)
. test age2 age3
  (1) [cvd]age2 = 0
  (2) [cvd]age3 = 0
         chi2(2) =
                    38.89
```

Prob > chi2 = 0.0000

Poisson Regression - Model and Coefficients

The LR test would use the same steps as earlier:

- 1. Run larger model (with age group vars and obesity), save log likelihood value (it is -17.083097)
- 2. Run model omitting age group vars, save likelihood value (it is -42.981143)
- 3. Compute D = -2(-42.981143 (-17.083097)) = 51.80
- 4. Result is larger than χ^2 with 2 df, then age variable(s) are significantly contributing to model fit

Both the Wald and LR test conclude: keep age variables

Poisson Regression - Model Fit

To help assess the fit of the model, the estat gof command can be used to obtain the goodness-of-fit χ^2 test. This is **not** a test of the model coefficients, but rather a test of the model form: Does the Poisson model form fit our data? Thus, large p-value indicates good fit.

```
Deviance goodness-of-fit = 3.49824
Prob > chi2(2) = 0.1739

Pearson goodness-of-fit = 3.525841
Prob > chi2(2) = 0.1715
```

A statistically significant (small p-value) here would indicate that the data do not fit the model well. In that situation, we may try to determine if there are omitted predictor variables, if our linearity assumption holds and/or if the conditional mean and variance of outcome are very different.

Poisson Regression - Model Fit

To see the basis of the fit test, we can look at observed vs, predicted values:

```
. predict cvd_pred
(option n assumed; predicted number of events)
```

. list AgeGroup ObesityStatus cvd cvd_pred, noobs clean

```
AgeGroup
          Obesit~s
                           cvd_pred
                     cvd
  60{64
             Obese
                      10
                           7.91759
  60{64
          Notobese
                      12
                           14.0824
  65{69
             Obese
                      34
                           40.10115
  65{69
          Notobese
                           38.89889
  70{74
             Obese
                           35.98157
  70{74
                           48.01822
          Notobese
```

- . gen chipart = (cvd cvd_pred)^2 / (cvd_pred)
- . tabstat chipart, stat(sum)

```
variable | sum
------
chipart | 3.52584
```

Note: This is the Pearson χ^2 sum that we compute for χ^2 tests in frequency tables

Fitting as a GLM

An alternative way to fit Poission regression is using the "glm" function (Stata or R), specifying which "family" to use (default is linear regression).

```
. glm cvd obstat age2 age3, family(Poisson) exposure(pyrs)
              log likelihood = -17.619973
Iteration 0:
              log likelihood = -17.083841
Iteration 1:
              log likelihood = -17.083097
Iteration 2:
              log likelihood = -17.083097
Iteration 3:
Generalized linear models
                                              Number of obs =
Optimization
                : ML
                                              Residual df
                                              Scale parameter =
                                              (1/df) Deviance = 1.74912
Deviance
             = 3.498240465
Pearson
             = 3.525841336
                                              (1/df) Pearson = 1.762921
Variance function: V(u) = u
                                               [Poisson]
Link function : g(u) = ln(u)
                                              [Log]
                                              AIC
                                                          = 7.027699
Log likelihood = -17.08309669
                                              BIC
                                                             = -.0852785
```

age2 1.223679 .2420611 5.06 0.000 .7492484 1.698111 age3 1.49372 .2397136 6.23 0.000 1.02389 1.96355	cvd	Coef.	OIM Std. Err.	Z	P> z	[95% Conf.	Interval]
_cons -3.816539 .219792 -17.36 0.000 -4.247323 -3.385754 ln(pyrs) 1 (exposure)	age2 age3 _cons	1.223679 1.49372 -3.816539	.2420611 .2397136 .219792	5.06	0.000	.7492484	.6753032 1.698111 1.96355 -3.385754

- Estimates are same as earlier. Again, β s are are in log(rates) on an additive scale.
- The overall fit statistics as well as other measures are provided.

Fitting as a GLM

The model executed in R:

```
> library(foreign)
> cvd <- read.dta("CVD_factors.dta")</pre>
> cvd
  AgeGroup ObesityStatus cvd pyrs agegrp obstat age2 age3 _est_nul _est_big
                                                                                 rate cvd_pred
     60{64
                                              1
                                                        0
                  Obese 10
                              245
                                                                1
                                                                          1 0.04081633 7.91759
1
     60{64
               Notobese 12
                             640
2
                                                        0
                                                                 1
                                                                         1 0.01875000 14.08240
     65{69
                             365
                                                                         1 0.09315068 40.10115
                   Obese 34
                                                1
                                                       0
                                                                1
                                                                         1 0.08653846 38.89889
4
     65{69
               Notobese 45
                              520
                                             0 1
                                                       0
                                                                1
    70{74
                             250
                                                       1
                                                                         1 0.16000000 35.98157
                   Obese 40
    70{74
                Notobese 44 490
                                       3
                                                  0
                                                       1
                                                                          1 0.08979592 48.01822
    chipart lnrate2
1 0.5476958 1.817766
2 0.3079306 1.857163
3 0.9282536 5.762812
4 0.9569315 7.195592
5 0.4487789 7.244460
6 0.3362491 7.103184
>
> Pois <- glm(cvd ~ offset(log(pyrs)) + obstat + age2 + age3, data=cvd, family=poisson)
```

```
>
> Pois
Call: glm(formula = cvd ~ offset(log(pyrs)) + obstat + age2 + age3,
    family = poisson, data = cvd)
Coefficients:
(Intercept)
                 obstat
                                age2
                                             age3
    -3.8165
                 0.3844
                              1.2237
                                           1.4937
Degrees of Freedom: 5 Total (i.e. Null); 2 Residual
Null Deviance:
                  65.08
Residual Deviance: 3.498 AIC: 42.17
```

Poisson Regression - summary measures

In SLR/MLR, we have a partition of variability captured by \mathbb{R}^2 . In Poisson regression (and other log-linear models), analogues to \mathbb{R}^2 have been sought. One simple one is

$$R_{pseud}^2 = 1 - \frac{\log L(\hat{\beta})}{\log \hat{L}_0}$$

where $\log L(\hat{\beta})$ is the log likelihood for the current model and $\log \hat{L}_0$ is the log likelihood for the null model.

ullet Generally, these measures are not as reliable as fits measures as in the linear regression setting (although R^2 can be misleading there too)

Poisson Regression - summary measures

Ex/ for the full model (age groups and obesity vs. null model we have

$$R_{pseud}^2 = 1 - \frac{-17.083096}{-47.874227}$$

$$= 1 - 0.3568 = 0.6432$$

As given in the output for the model of interest:

```
. poisson cvd obstat age2 age3, exposure(pyrs) irr
. . .
```

Poisson regression	Number of obs	=	6
	LR chi2(3)	=	61.58
	Prob > chi2	=	0.0000
Log likelihood = -17.083097	Pseudo R2	=	0.6432

. . . .

Alternate Models

Fit the Negative Binomial model (note: for this dist'n, variance increases as mean increases)

```
. nbreg cvd obstat age2 age3, exposure(pyrs)
Fitting Poisson model:
Iteration 0:
               log\ likelihood = -17.107802
Iteration 1:
               log likelihood = -17.083109
               log\ likelihood = -17.083097
Iteration 2:
               log\ likelihood = -17.083097
Iteration 3:
Fitting constant-only model:
Iteration 0:
               log likelihood = -26.909909
               log\ likelihood = -25.989194
Iteration 1:
               log\ likelihood = -25.570977
Iteration 2:
               log likelihood = -25.567453
Iteration 3:
               log\ likelihood = -25.567453
Iteration 4:
```

Fitting full model:

```
log\ likelihood = -22.857883
Iteration 0:
               log likelihood = -19.909726
Iteration 1:
               log likelihood = -19.73484
                                            (not concave)
Iteration 2:
Iteration 3:
               log likelihood = -19.347292
                                            (not concave)
Iteration 4:
               log\ likelihood = -17.635909
               log\ likelihood = -17.197221
Iteration 5:
Iteration 6:
               log likelihood = -17.112039
Iteration 7:
               log\ likelihood = -17.089736
Iteration 8:
               log\ likelihood = -17.084648
               log\ likelihood = -17.083448
Iteration 9:
               log\ likelihood = -17.083167
Iteration 10:
               log likelihood = -17.083109
Iteration 11:
               log likelihood = -17.083098
Iteration 12:
Iteration 13: log likelihood = -17.083096
                                            (not concave)
Iteration 14: log likelihood = -17.083096
Negative binomial regression
                                                Number of obs
                                                                             6
                                                LR chi2(3)
                                                                         16.97
                                                                        0.0007
Dispersion
                                                Prob > chi2
               = mean
Log likelihood = -17.083096
                                                Pseudo R2
                                                                        0.3318
         cvd |
                    Coef. Std. Err.
                                                P>|z|
                                                          [95 Conf. Interval]
                                          Z
      obstat |
               .3843709
                             .148442
                                         2.59
                                                0.010
                                                          .0934299
                                                                      .6753118
```

```
1.223679
                           5.06
                                                1.69811
     age2 |
                   .2420612
                                0.000
                                     .7492478
     age3 |
          1.493717
                   .2397137 6.23
                                     1.023887
                                0.000
                                               1.963547
    _cons | -3.816542
                   .2197921
                          -17.36
                                0.000
                                      -4.247327
                                               -3.385758
  ln(pyrs) |
                1 (exposure)
  /lnalpha | -18.60187 1339.439
                          -2643.855
                                               2606.651
    alpha | 8.34e-09 .0000112
```

Note: Poisson is a special case when $\alpha=0$ - test above is for $H_0:\alpha=0$, which is NOT rejected. This means Poisson model is adequate. Parameters are very similar to Poisson model fit earlier.

Summary – Poisson Regression and GLMs

The Poisson data-based model provided a strong inferential and data exploratory tool for events in relation to person-time of exposure

When there seems to be an issue of bad fit, we should first check if our model is appropriately specified, such as omitted variables and functional form, and then consider variations on the model that may fit better

The Poisson provides a bridge between linear regression, discrete event counts, and rates of failure, which relates to time to event (survival) data

Summary – Courses Beyond Linear Regression

This course will briefly introduce variations on linear regression. Further development of these methods and others are extensively covered in other University of Chicago courses such as:

- Categorical (Discrete) Data Analysis all types of discrete outcome variables - binomial, multinomial, ordinal, counts
- Generalized Linear Models all GLMs
- Biostatistical Methods logistic, Poisson, hazard (failure rate, time to event) in health science context
- Applied Survival Analysis analysis of time to event data, including regression methods for these data
- ullet Applied Longitudinal Data Analysis extending regression to repeated measurements on Y