PBHS 32100 / STAT 22401 Winter 2025 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 when comparing groups

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	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	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 only, 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

I	obstat		1		
I	Exposed	Unexposed	Total		
+			-+		
cvd	84	101	185		
pyrs	860	1650	2510		
+			-+		
Incidence rate	.0976744	.0612121	.0737052		
I			1		
I	Point	estimate	[95% Conf	. Interval]	
I			-+		
<pre>Inc. rate diff. </pre>	.03	364623	.0124039	.0605207	
Inc. rate ratio	1.5	595671	1.180226	2.15264	(exact)
Attr. frac. ex.	.37	' 33045	.1527047	.535454	(exact)
Attr. frac. pop	. 16	395004	1		
+					

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	•	Std. Err.				Interval]
_cons	1.595671	.2356291 .0060908	3.16	0.002	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 $.6125 \times 1.5956 = .09767$ 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	cvd	pyrs
60{64 65{69 70{74	79	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	IRR	Std. Err.	z	P> z	[95% Conf.	Interval]
obstat agegrp _cons ln(pyrs)	1.871195 .0162154	.1845068	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 agegrp = 0 (not particularly useful)
- b. $\beta_{agegrp} = 1.87$ Indicating a 1.87-fold increase in CVD rate per age group increase (1x for group 1, 2x for group 2, 3x for group 3)
- c. $\beta_{obstat}=1.535$ Indicating a 1.54-fold increase in CVD for obese vs. nonobese- similar to effect seen earlier before adding age

Rates produced for three age groups are:

Nonobese: 0.036, 0.067, 0.127

Obese: 0.055, 0.102, 0.195

Poisson Regression - Categorical Predictor for Age

. 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	=	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
	<pre>ln(pyrs) </pre>	1	(exposure)				

Note: _cons estimates baseline incidence rate.

Poisson Regression - Categorical Predictor for Age

	cvd	IRR	Std. Err.	z	P> z	[95% Conf.	Interval]
obs	stat	1.468678	.2180134	2.59	0.010	1.097924	1.964629
a	ige2	3.399674	.8229289	5.06	0.000	2.115409	5.463615
a	ige3	4.453633	1.067596	6.23	0.000	2.784004	7.124574
_c	ons	.0220038	.0048363	-17.36	0.000	.0143025	.0338521
ln(py	rs)	1	(exposure)				

Note: _cons estimates baseline incidence rate.

This model may be closer to table-based rates, but different here because separate by obesity

Rates produced for three age groups are:

Nonobese: 0.022, 0.075, 0.098

Obese: 0.032, 0.109, 0.144

The CVD data was aggregated by groups (age, obesity) with event counts in the groups

- We can also work with individual case data, where each individual either does or does not have the event (coded 0 or 1) over some recorded follow-up time for that individual
- Total person-time and the tally of events produces the overall rate
- Person-time and event counts within covariate groups produces rates according to covariates

Ex/ Endometrial cancer among women receiving tamoxifen/placebo in a breast cancer clinical trial.

- Tamoxifen is an anti-estrogen that is highly effective in treatment of breast cancer. Tamoxifen binds to estrogen receptors on the tumor and arrests growth.
- Approved for use across a spectrum of the disease from metastatic to early stage and DCIS, and even in cancer prevention among women deemed at high risk
- Tamoxifen is associated with increased risk of endometrial (uterine) cancer. The benefits are generally considered to outweigh the risk for treatment. In prevention, it is a larger concern

Data from the NSABP B-14 tamoxifen trial (N-, ER+ breast cancer): Endometrial cancer was uncommon (16 cases) relative the the studied group (N > 2800) and amount of follow-up time (10+ years):

. list id trt menstat age bmi endo timefree, clean

id	trt	menstat	age	bmi	endo	timefree
359	1	3	59	23.2	0	189.8
362	1	1	36	27.4	0	41.3
364	1	3	55	18.6	0	122.4
366	1	3	55	30.6	0	9.9
367	2	3	58	23.4	1	95
371	1	2	49	22.1	0	39.5
374	2	3	63	25.1	0	199.5

. . . .

. . . .

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

. ir endo trtx timefree Incidence-rate comparison trtx | Exposed Unexposed | endo | 13 16 timefree | 90322.5 79946.1 | 170268.6 Incidence rate | .0001439 .0000375 | .000094 Point estimate | [95% Conf. Interval] .0001064 | .0000174 .0001954 Inc. rate diff. | Inc. rate ratio | 3.835513 | 1.053989 20.98384 (exact) Attr. frac. ex. | .7392787 | .0512237 .9523443 (exact) Attr. frac. pop | .6006639

Use Poisson model:

```
. poisson endo trtx, exposure(timefree)
Iteration 0: log likelihood = -93.429861
Iteration 1: log likelihood = -93.428424
Iteration 2: log likelihood = -93.428424
```

Poisson regression	Number of obs	=	1,395
	LR chi2(1)	=	5.58
	Prob > chi2	=	0.0182
Log likelihood = -93.428424	Pseudo R2	=	0.0290

endo	Coef.	Std. Err.	z	P> z	[95% Conf.	Interval]
	-10.1905	.6405126 .5773502 (exposure)			.0889214 -11.32208	2.599685 -9.05891

[.] 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 regression				Number		=	1,395
				LR chi2	(3)	=	8.06
				Prob >	chi2	=	0.0448
Log likelihood		Pseudo 1	R2 	=	0.0419		
endo	IRR	Std. Err.	z	P> z	[95%	Conf.	Interval]
trtx	3.715235	2.381092	2.05	0.041	1.057	917	13.04731
age	1.032185	.0297447	1.10	0.272	.9755	024	1.092161
bmi	1.040999	.0452663	0.92	0.355	.9559	539	1.133609
_cons	2.23e-06	4.38e-06	-6.62	0.000	4.71e	e-08	.0001052
<pre>ln(timefree) </pre>	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:

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

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 linear regression.

To illustrate, 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
                                                                            6
                                                LR chi2(0)
                                                                         -0.00
                                                Prob > 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
                                                Number of obs
Poisson regression
                                                                             6
                                                LR chi2(3)
                                                                        61.58
                                                Prob > chi2
                                                                        0.0000
```

Pseudo R2

0.6432

Log likelihood = -17.083097

. . .

. * SAVE it

. est store big

•

.* CONTRAST these models

. lrtest big nul

Likelihood-ratio test
(Assumption: nul nested in big)

LR chi2(3) = 61.58

Prob > chi2 = 0.0000

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. This means (some) predictors matter.

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 regres	ssion			Number of	obs =	6
				LR chi2(3	3) =	61.58
				Prob > ch	ni2 =	0.0000
Log likelihood	d = -17.08309	7		Pseudo R2	2 =	0.6432
cvd	•	Std. Err.	z	P> z	[95% Conf.	Interval]
obstat		.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.

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
                          cvd_pred
  60{64
             Obese
                      10
                           7.91759
  60{64
                          14.0824
          Notobese
                     12
  65{69
                          40.10115
             Obese
                      34
   65{69
          Notobese
                          38.89889
  70{74
                          35.98157
             Obese
  70{74
                           48.01822
          Notobese
                      44
```

- . 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)
```

```
Iteration 0: log likelihood = -17.619973
Iteration 1: log likelihood = -17.083841
Iteration 2: log likelihood = -17.083097
Iteration 3: log likelihood = -17.083097
```

Generalized linear	models	Number of obs	=	6
Optimization :	ML	Residual df	=	2
		Scale parameter	=	1
Deviance =	3.498240465	(1/df) Deviance	=	1.74912
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

0I cvd Coef. Std.	Err. z	P> z	[95% Conf.	Interval]
obstat .3843624 .1484 age2 1.223679 .2420 age3 1.49372 .2397 _cons -3.816539 .219 ln(pyrs) 1 (expos	0611 5.06 7136 6.23 9792 -17.36	0.000	.0934215 .7492484 1.02389 -4.247323	.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
    60{64
                                             1
1
                  Obese 10 245
                                                       0
    60{64
2
               Notobese 12 640
                                             0
                                                       0
3
    65{69
                  Obese 34 365
                                            1 1
                                                      0
    65{69
               Notobese 45 520
                                            0 1
4
                                                      0
5
    70{74
                  Obese 40 250
                                                 0
                                                      1
6
    70{74
               Notobese 44 490
                                      3
                                             0
                                                  0
                                                      1
>.
>
> 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 when Poisson does not appear to be correct model

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
Iteration 2: log likelihood = -17.083097
Iteration 3: log likelihood = -17.083097
```

Fitting constant-only model:

```
Iteration 0: log likelihood = -26.909909

Iteration 1: log likelihood = -25.989194

Iteration 2: log likelihood = -25.570977

Iteration 3: log likelihood = -25.567453

Iteration 4: log likelihood = -25.567453
```

Fitting full model:

```
Iteration 0:
               log likelihood = -22.857883
               log likelihood = -19.909726
Iteration 1:
               log likelihood = -19.73484
                                           (not concave)
Iteration 2:
               log likelihood = -19.347292
Iteration 3:
                                            (not concave)
               log\ likelihood = -17.635909
Iteration 4:
Iteration 5:
               log\ likelihood = -17.197221
               log\ likelihood = -17.112039
Iteration 6:
Iteration 7:
               log likelihood = -17.089736
               log\ likelihood = -17.084648
Iteration 8:
Iteration 9:
               log\ likelihood = -17.083448
Iteration 10:
               log\ likelihood = -17.083167
Iteration 11:
               log likelihood = -17.083109
Iteration 12: log likelihood = -17.083098
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
Dispersion
                                                                       0.0007
                                               Prob > chi2
               = mean
Log likelihood = -17.083096
                                               Pseudo R2
                                                                       0.3318
                   Coef. Std. Err. z > |z|
                                                         [95 Conf. Interval]
         cvd |
```

obs	tat	.3843709	.148442	2.59	0.010	.0934299	.6753118
a	ge2	1.223679	.2420612	5.06	0.000	.7492478	1.69811
a	ge3	1.493717	.2397137	6.23	0.000	1.023887	1.963547
_c	ons	-3.816542	.2197921	-17.36	0.000	-4.247327	-3.385758
ln(py	rs)	1	(exposure)				
/lnal	+- pha +	-18.60187	1339.439			-2643.855	2606.651
al	, pha 	8.34e-09	.0000112			0	
LR test of alpha=0: chibar2(01) = 6.8e-07				Prob >= chiba	ar2 = 0.500		

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 introduces a few common 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