



Marcello Pagano

[JOTTER 11 LOGISTIC REGRESSION]

Odds ratio, logistic function, dichotomous response, weighted least squares



This week we stay on our theme of regression and we are going to talk about logistic regression—we extend the idea of regression to the situation where our outcome variable is dichotomous.

To introduce the topic we look at a famous cartoon by James Gillray in 1802¹. It deals with the reaction to what at the time was the rather revolutionary idea of vaccination. This was the first time a disease from another species was injected into man for beneficial purposes. To make the point of the anti-vaccine crowd, you see various ways of caricaturing the practice, by having cows protrude from all sorts of places.

TABLE SHOWING NUMBER OF SMALL-POX CASES (948 VACCINATED AND 220 UNVACCINATED)
AT EACH AGE-PERIOD, WITH RELATIVE DEGREES OF SEVERITY.

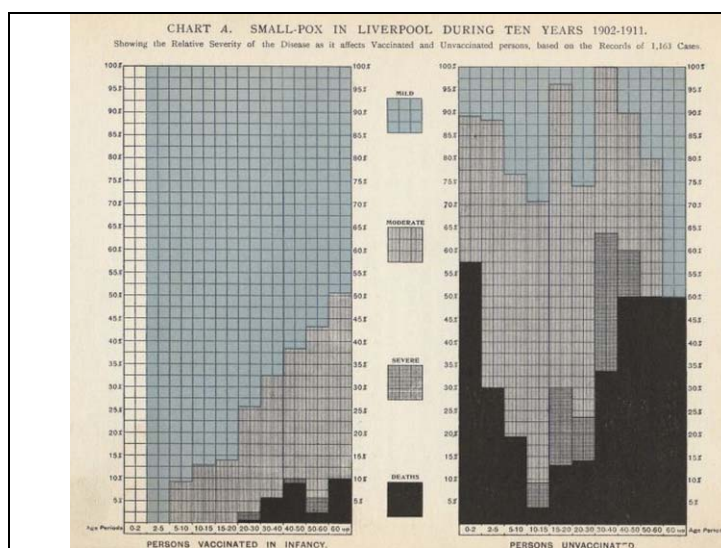
	Under 5 years		5-9		10-14		15-19		20-24		25-29		30-34		35-39		40 and up		Total			
	Vac.	Un- vac.	Vac.	Un- vac.	Vac.	Un- vac.	Vac.	Un- vac.	Vac.	Un- vac.	Vac.	Un- vac.	Vac.	Un- vac.	Vac.	Un- vac.	Vac.	Un- vac.	Vac.	Un- vac.		
A. Modified discrete and discrete	No cases	3	7	3	31	6	54	9	89	1	249	11	163	No cases	63	1	20	2	10	1	686	37
B. Profuse discrete and semi- confluent	No cases	9	No cases	15	3	15	8	19	14	20	77	21	72	5	29	3	13	3	8	No cases	224	110
C. Confluent and death	No cases	17	No cases	5	No cases	5	No cases	3	No cases	9	7	10	13	9	9	6	2	5	2	1	33	73
Total	No cases	29	7	26	34	26	62	31	101	30	333	42	248	14	101	10	35	10	20	2	943	220
Deaths also	0	17	0	8	0	5	0	1	0	4	3	6	13	8	9	5	1	5	2	1	28	60

William Hanna, Studies in Smallpox and Vaccination,
William Wood and Company, New York 1913.

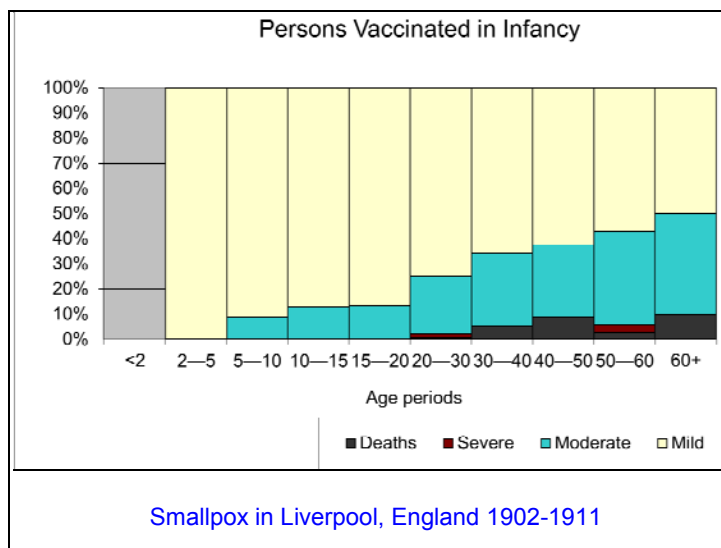
William Hanna, Studies in Smallpox and Vaccination,
William Wood and Company, New York 1913.

¹ *The Cow-Pock or the Wonderful Effects of the New Inoculation* by James Gillray (1757-1815) was published in England on June 12, 1802 by the Anti-Vaccine Society.

Smallpox was a quite lethal problem at that time, 200 years ago, as it was even 100 years ago, when this book was written². It gives a thorough statistical description of a smallpox outbreak in the city of Liverpool that was part of a general outbreak they had in England in 1902-1903.



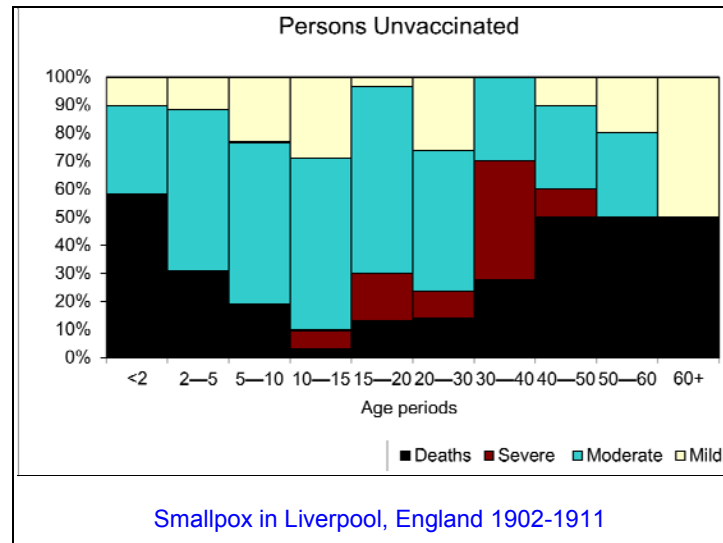
Above is a graphic from the book. It shows, as a function of age, the health impact of the epidemic. The panel on the left is for people who had been vaccinated at birth, and the panel on the right is for those not so vaccinated. One hundred years after the cartoon, vaccination had taken hold, although not everyone was vaccinated. The black bars show the number of people who died, by age. So you can see that the number of deaths is very much less for those who were vaccinated.



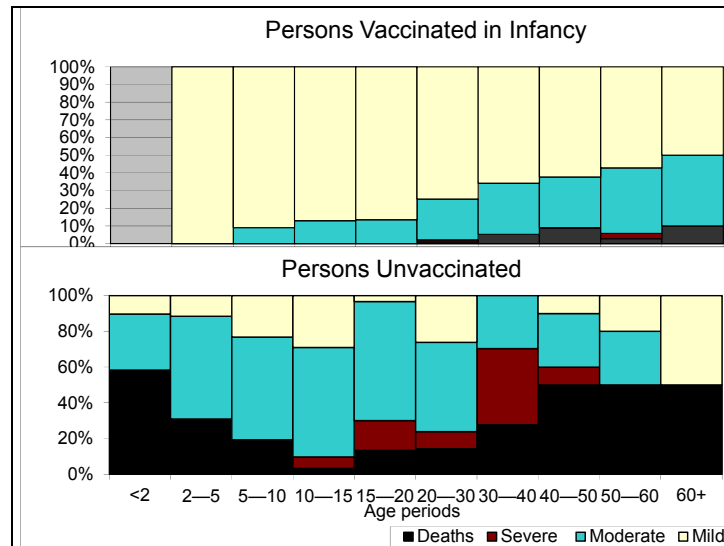
What I did was I reproduced those two graphs using modern techniques. This graph is for those who were vaccinated—the left panel above. Just focusing on the deaths we see a slight trend as people age.

² William Hanna, Studies in Smallpox and Vaccination, William Wood and Company, New York 1913.

Also, if we look at the frequencies of “Moderate” effects, those too increase with age. All in all, what we see is consonant with the beliefs that the effects of vaccinations wear off with time—most of these individuals were vaccinated shortly after birth.



For those unvaccinated, we see a large number of deaths—much more black on the graph than for the previous one.

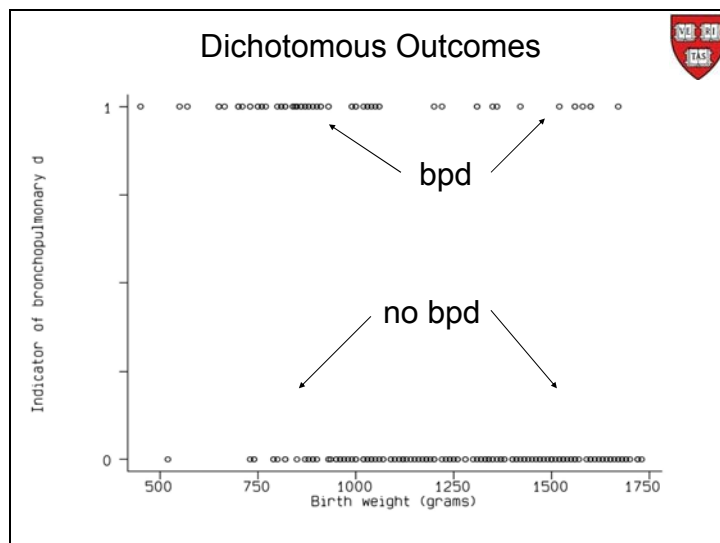


Indeed, if we place these two together, we can see that there is a big difference between the two graphs, arguing that vaccination has a great beneficial effect.

Focusing on the Vaccinated, if we look at the proportion who die in each age group we see an age effect. Certainly with the young ones, nobody below the age of 20 dies. Also, looking at the percentage who suffer Moderate, or worse, effects those too build up with age.

Age	Vaccinated			Unvaccinated		
	Numb.	Died	Mortal	Numb.	Died	Mortal
<2	0	0	0	29	17	58.0%
2—5	7	0	0	26	8	30.6%
5—10	34	0	0	26	5	19.0%
10—15	62	0	0	31	1	3.2%
15—20	103	0	0	30	4	13.3%
20—30	333	3	0.9%	42	0	14.2%
30—40	248	13	5.2%	14	8	33.3%
40—50	101	9	8.9%	10	5	50.0%
50—60	35	1	2.8%	10	5	50.0%
≥60	20	2	10.0%	2	1	50.0%
Total	943	28	2.9%	220	60	27.2%

What we are seeing is that the probability, or the proportion, who are dying is impacted by age. This reminds us of regression—we can regress the proportion who die on age. And here are the numbers to support this suggestion. If we look at the vaccinated we can see that the mortality goes up with age, almost monotonically. It is not quite smooth because of the 50 to 60 age group, but it does seem like age might affect the mortality rate, in general. Of course, we now know that the effect of vaccination does wear off with time—vaccination occurred in infancy.



Here is another example. We are looking at babies who suffer from bpd (bronchopulmonary dysplasia). This condition gets measured at about age 29 days, roughly a month after birth, amongst premature infants, and it indicates progressive lung inflammation. This study³ was carried out on infants born weighing less than 1750 grams and each child was categorized as 0 (no bpd), or 1 (bpd) and the results are plotted above, as a function of birth age.

We can see that at the left of the graph (low birth weight) we see a higher intensity of infants with bpd, whereas on the right (relatively higher birth weight) we see a higher intensity of infants without bpd. This picture would be indicative of what we would expect to see if the probability of bpd goes down as birth weight increases. There are kids with and without bpd at either end of the scale, so we are not observing a phenomenon that deterministically decides the classification, but rather something more nuanced.

For example, if we create a window of width 250 grams, say, and slide this window from left to right, then the *proportion* of babies in the window who have bpd will go down as we move across.

³ Van Marter, L. J., Leviton, A., Kuban, K. C. K., Pagano, M., and Allred, E. N., Maternal Glucocorticoid Therapy and Reduced Risk of Bronchopulmonary Dysplasia," *Pediatrics*, **86**, September 1990, 331-336.

Bpd by birth weight



Birthweight (gms)	Bpd	N	Prop.	Odds
0-950	49	68	0.721	2.58
951-1350	18	80	0.225	0.29
1351-1750	9	75	0.120	0.14
Total	76	223	0.341	0.52

A simple manifestation of this idea would be to take a snapshot of the window in three locations. Here I have arbitrarily chosen these three intervals, for no other reason than to make this point: the proportion with bpd goes down as we go from top to bottom. That means, as the birth weight increases. This behavior, of course, is evident in the odds of bpd, too—they go down as birth weight increases. The challenge is to be somewhat more formal in quantifying this relationship between the probability, or odds, of bpd and birth weight.

Logistic regression



In linear regression, continuous Y:

$$\mu_{Y|x} = \alpha + \beta x$$

In case of dichotomous Y:

$$\mu_{Y|x} = \Pr(Y = 1 | x) = p_{Y|x}$$

$$1. \quad p_{Y|x} = \alpha + \beta x$$

$$2. \quad p_{Y|x} = e^{\alpha + \beta x}$$

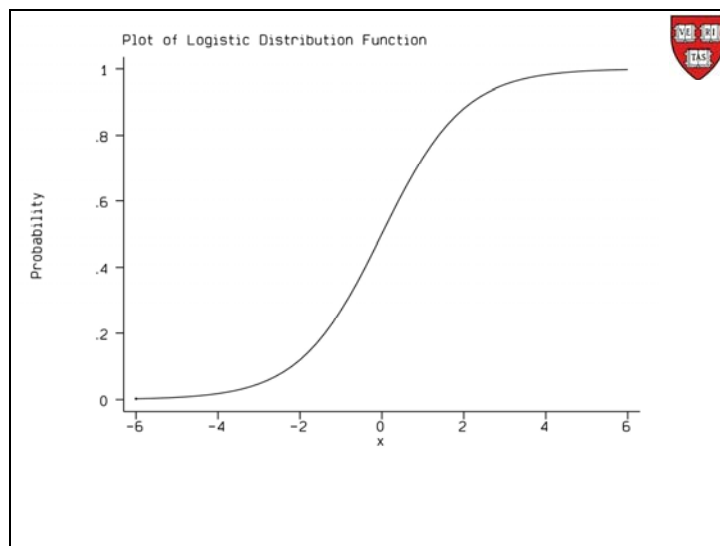
$$3. \quad p_{Y|x} = \frac{e^{\alpha + \beta x}}{1 + e^{\alpha + \beta x}}$$

Linear regression allowed us to quantify the relationship between a response variable and explanatory variables. For example, with simple linear regression, the regression line was the straight line relationship between the mean of the Ys and the explanatory, x.

We can mimic what we did there by first calculating the mean of the Ys. Now Y is a Bernoulli variable that takes on the values 0 and 1, so we know that its mean is the probability that it takes on the value 1. So suggestion 1, would have us fitting a straight line to that probability. That is clearly unsatisfactory because for one a straight line can be negative. So suggestion 2 would have us taking the exponential of the

straight line—that would solve the problem about becoming negative. Unfortunately, that still leaves us with the problem that this function can be greater than one and thus would not be a good model for a probability.

Suggestion 3 satisfies all the constraints on a probability. Not only that, it is monotonic in x —that means that the probability goes up with x (as x gets larger, the probability gets larger) or the probability goes down with x (as x gets larger the probability gets smaller). One can prove this mathematically, or you can convince yourself by drawing this function for yourself. You will then also see that what determines whether it goes up with x getting larger, or down with x getting larger, is the sign of the β —positive β means probability goes up with x getting larger. Note, of course, that if $\beta=0$, then the probability is not impacted by the value of x . In that case we would conclude that Y is independent of X .



If we plot this as a function of x , it looks something like this— $\alpha=0$ and $\beta=1$ in this case. This is what the logistic function looks like for a positive β . If $\beta<0$, then we get the mirror image of this function that starts at one in the top-left corner and monotonically decreases to zero in the bottom right-hand corner—in other words, one minus this function.

So if we were to use this function to model the probability of bpd as a function of birth weight, we would expect a negative β . Of course, we could have switched the roles of zero and one in the definition of bpd, and then we would expect a positive β , as drawn above, because then the curve would represent the probability of *not* having bpd.

Log odds and logistic

If $p_{y|x} = \frac{e^{\alpha + \beta x}}{1 + e^{\alpha + \beta x}}$

then

$$\ln \left(\frac{p_{y|x}}{1 - p_{y|x}} \right) = \alpha + \beta x$$

e.g. Log odds =

$$\ln \left(\frac{p_{bpd|bwt}}{1 - p_{bpd|bwt}} \right) = 4.0343 - 0.0042 \times bwt$$

where $p_{bpd|bwt}$ is the probability of bpd for a given birthweight (bwt).

If we solve the logistic function for $\alpha + \beta x$ we get the above equation for the log odds. So, simple logistic regression fits a straight line to the log of the odds.

So for example, in our bpd example, the straight line that we would fit to the log odds has intercept 4.03 and slope -0.0042. These numbers were obtained by using least squares to fit the line to the data. To be precise, it is not the least squares we are accustomed to using but, since we do not have homoscedasticity, we need to use a technique called weighted least squares. Another approach, that yields the same answer, is what is called, maximum likelihood. The technicalities associated with both are beyond the scope of this course, but this is what Stata calculates for us.

Stata:

In model form....beta

```
. logit bpd birthwt
```

```
Iteration 0:  log likelihood = -143.06998
Iteration 1:  log likelihood = -113.06062
Iteration 2:  log likelihood = -111.86443
Iteration 3:  log likelihood = -111.86031
Iteration 4:  log likelihood = -111.86031
```

Logistic regression

Number of obs	=	223
LR chi2(1)	=	62.42
Prob > chi2	=	0.0000
Pseudo R2	=	0.2181

Log likelihood = -111.86031

	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
birthwt	-.0042291	.0006409	-6.60	0.000	-.0054852 - .0029731
_cons	4.034291	.6957851	5.80	0.000	2.670578 5.398005

There are two Stata commands we can use. One is *logit* and it works very much like *regress*, and the output we get looks quite similar to what we get with *regress*, and it is interpreted much the same way.

So, in this case, we get that birth weight is significant. We see that the 95% confidence interval does not include zero, and since the coefficient is negative we conclude that, as birth weight goes up, the odds, or the probability, of getting BPD goes down. The log of the odds of getting bpd goes down by 0.0042 for every gram increase in birth weight.

Stata:

In odds form....odds ratio

```
. logistic bpd birthwt
```

Logistic regression

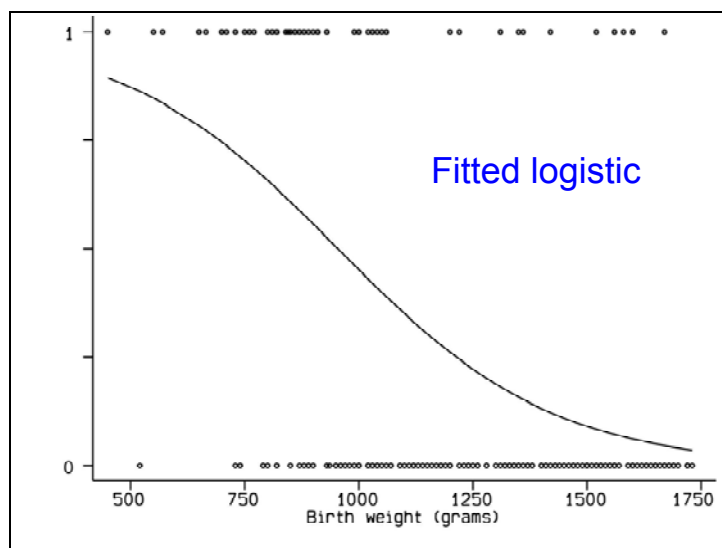
Log likelihood = -111.86031

Number of obs = 223
 LR chi2(1) = 62.42
 Prob > chi2 = 0.0000
 Pseudo R2 = 0.2181

	bpd	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
birthwt		.9957798	.0006382	-6.60	0.000	.9945298 .9970313
_cons		56.50287	39.31386	5.80	0.000	14.44831 220.9652

We can look at the odds directly by using the other command in Stata to fit this model, and that is the command *logistic*. It reports the odds ratio, rather than reporting the betas. Remember, we are fitting the straight line to the log of the odds, so if we report the odds that is the same as reporting the exponentials of the last screen. That means, for example, that for every gram increase in birth weight, the odds of getting bpd gets multiplied (because we are taking the exponentials) by 0.9957798. (The $\log(0.9957798) = -0.0042291$.)

The interpretation, of course, does not change, it is just a different way to report the same results.



Here is the fitted logistic. So if we had an idealized version of the moving window we described earlier, then as it moves from left to right, this curve shows the proportion in the window with bpd.

Stata:

In model form....beta

```
. logit bpd birthwt
```

Iteration 0: log likelihood = -143.06998
 Iteration 1: log likelihood = -113.06062
 Iteration 2: log likelihood = -111.86443
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 Iteration 4: log likelihood = -111.86031

Logistic regression

Log likelihood = -111.86031

Number of obs = 223
 LR chi2(1) = 62.42
 Prob > chi2 = 0.0000
 Pseudo R2 = 0.2181

	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
bpd					
birthwt	-.0042291	.0006409	-6.60	0.000	-.0054852 -.0029731
_cons	4.034291	.6957851	5.80	0.000	2.670578 5.398005

Returning to the beta coefficients, we see that the coefficient of birth weight is small. The units of this are 1/grams, so if we were to measure the babies' birth weights in Kilograms, this coefficient would become -4.2291. One should be cognizant of the units of the measurement before opining about its size.


Observed versus fitted

Birthweight (gms)	Obsrvd bpd	Fitted bpd	N
0-950	0.721	0.646	68
951-1350	0.225	0.324	80
1351-1750	0.120	0.082	75
Total	0.341	0.341	223

One way to judge how well the model has done is to return to trichotomy we created before. In green we see the observed proportions. For each child we also now have a fitted probability of getting bpd—for a child weighing x grams, solve for p in the equation: the $\log(p/(1-p)) = 4.034291 - 0.0042291 \times x$. The red numbers above are the averages of these p for the babies in the respective groups.

So the “fitted” values compare somewhat with the actual, observed values. There is some room for improvement.

Back to Liverpool 1902-11, vaccinated



```

. blogit dead total age, or
Logistic regression for grouped data
Log likelihood = -116.26154
Number of obs   =    943
LR chi2(1)      =   19.58
Prob > chi2     =   0.0000
Pseudo R2      =   0.0777


```

_outcome	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
age	1.064589	.0147107	4.53	0.000	1.036144	1.093816
_cons	.00361	.0020815	-9.75	0.000	.0011661	.0111764

Returning to the Liverpool outbreak, we can fit a logistic model to those data. Unfortunately, we did not have the raw data, only what we presented above, so in the reconstruction we had to cheat a little bit since we only know the ages within a category. What we did is take the midpoint of each category and used that to represent the age of all the individuals in that category. Now that we have so called *blocked* data—we have data only in blocks, not individual data—we can use the Stata command called *blogit*, it is the command to use for data presented in this fashion.

So here are the results for such a logistic analysis on the people who had been vaccinated prior to the outbreak in Liverpool. This says that the odds are multiplied by 1.06 every time we go up one year in age. We see that this is significant, so that age is an important explanatory variable.

Logistic growth model



Aside, population models from human ecology:

r is net population growth rate per individual

N_t is the population size at time t

$$N_{t+1} - N_t = r N_t$$

(Malthus, doubles every 25 years) — exponential growth

If K is number sustainable by environ

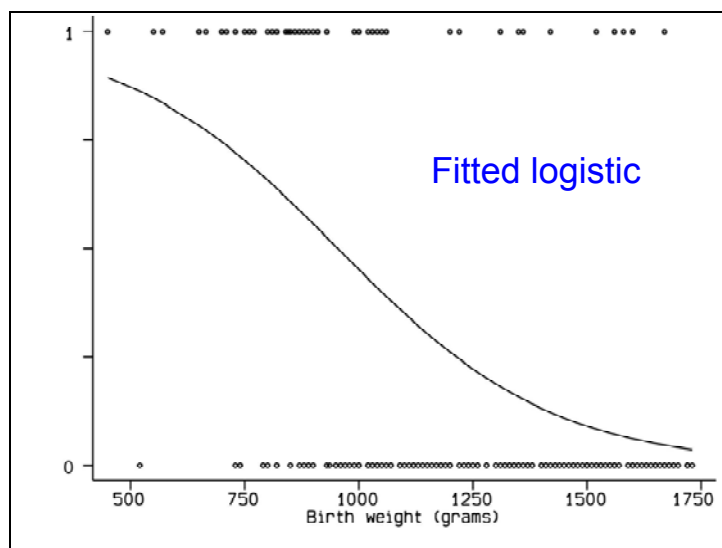
$$N_{t+1} - N_t = r N_t (1 - N_t / K) \quad \text{— logistic growth}$$

As an aside, I just wanted to point out that the logistic growth model also does appear in ecology. If you look at population size at time t , call that N_t . Suppose each individual in the population gives birth to r individuals in the next generation. Then if you look at the population growth, we see that expressed in the equation above.

This is what Malthus was concerned about almost two centuries ago, because the r he envisioned led to a doubling of the population approximately every 25 years. He was quite prescient. And that is worrisome. The value of r is all important: if r is less than 1, then we will eventually die out; r is equal to 1, then we just remain the same size; and, if r is bigger than 1, then that leads to exponential growth.

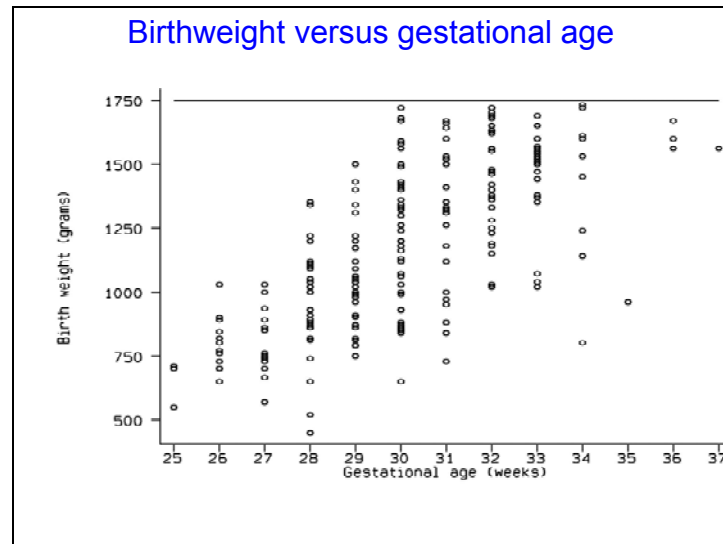
Now what happens to this model if the surroundings cannot maintain the exponential growth? For example, suppose you can only sustain K individuals in your environment. Incorporating that constraint into the growth model leads to logistic growth.

Multiple Logistic



So we fitted the logistic to a single variable—birth weight—and found that the fit was good, but it left some room for improvement. Logistic regression works just like linear regression. We can do simple logistic regression with a single variable, and we can increase the number of explanatory variables to get multiple logistic regression.

We run into exactly the same problems we had with multiple linear regression: which explanatory variable will be best? Is there room for other explanatory variables? What about interaction? What about multicollinearity? And we handle them in a manner very similar to the way we did in the case of linear regression.



Consider two candidates for inclusion in the regression as explanatory variables; birth weight and gestational age. Here is a scatter plot of these two. We definitely see a relationship between the two even with the study cutoff that the babies had to weigh less than of 1750 grams at birth. This relationship is, of course, of no surprise.

So instead of birth weight, we could consider incorporating gestational age as an explanatory variable.

Bpd by gestational age:

Gestational age	bpd	n	Proport.
<29 wks	40	58	0.690
29—30 wks	26	73	0.356
>30 wks	10	92	0.109

Does this yield information over and above birth weight?

Once again, for exploratory purposes, let us break down the gestational age into three categories. As expected, we see a “dose response”, or monotonic relationship with proportion with bpd. A high proportion (69%) in the smallest gestational age group, have bpd. A smaller proportion (35.6%) in the middle age group, have bpd. The smallest proportion (10.9%) with bpd is in the group with the biggest gestational ages. We thus see evidence of a decrease in the chance of having bpd with gestational age.

Birthweight by gestational age



Percent with bpd:

Birth wt (gms)	Gestational age (weeks)		
	<29	29-30	>30
0-950	0.805 (n=41)	0.714 (n=21)	0.167 (n=6)
951-1350	0.412 (n=17)	0.194 (n=36)	0.148 (n=27)
1351-1750	- (n=0)	0.250 (n=16)	0.085 (n=59)

Before entering the gestational age as an explanatory variable, let us check for collinearity between gestational age and birth weight. Consider this 3-by-3 table. Once again, this is just for expository purposes, but if we had collinearity we would expect to only have single entries in a row—for example, just entries in the diagonal cells—certainly not entries in all cells but one. Indeed, in each row we see a monotonic decrease in the proportion with bpd, thus arguing that even accounting for birth weight, we see an impact of gestational age.

Having this exploratory investigation under our belts, let us fit the model with both explanatory variables.


```
. logit bpd birthwt gestage
```

```
Iteration 0:  log likelihood = -143.06998
Iteration 1:  log likelihood = -106.45551
Iteration 2:  log likelihood = -104.6221
Iteration 3:  log likelihood = -104.6146
Iteration 4:  log likelihood = -104.6146
```

```
Logistic regression              Number of obs   =      223
                                LR chi2(2)         =      76.91
                                Prob > chi2         =      0.0000
Log likelihood = -104.6146        Pseudo R2       =      0.2688
```

	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
birthwt	-.0024097	.0007925	-3.04	0.002	-.003963	-.0008564
gestage	-.3982616	.1129995	-3.52	0.000	-.6197366	-.1767865
_cons	13.02725	2.932117	4.72	0.000	8.000408	19.57409

Here is the output from Stata. As expected, we see that both coefficients are negative, so the chances of bpd go down as either birth weight or gestational age goes up. Both p values are less than 0.05, so both are considered significant. Of course, we could have arrived at the same conclusion by looking at the two confidence intervals.




```

. logistic bpd birthwt gestage
Logistic regression
Log likelihood = -104.6146
Number of obs   =    223
LR chi2(2)      =    76.91
Prob > chi2     =    0.0000
Pseudo R2      =    0.2688

```

	bpd	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
birthwt		.9975932	.0007906	-3.04	0.002	.9960448 .9991439
gestage		.6714864	.0758777	-3.52	0.000	.5380862 .8379587
_cons		1011810	2966744	4.72	0.000	3230.552 3.17e+08

We could have come to the same conclusion with the *logistic* command.




Red is observed bpd proportion, green is fitted

Birth wt (gms)	Gestational age (weeks)		
	<29	29-30	>30
0-950	0.805	0.714	0.167
	0.766	0.514	0.320
	(n=41)	(n=21)	(n=6)
951-1350	0.412	0.194	0.148
	0.527	0.354	0.152
	(n=17)	(n=36)	(n=27)
1351-1750	-	0.250	0.085
	-	0.162	0.085
	(n=0)	(n=16)	(n=59)

To investigate the fit, we can repeat the exercise we carried out above with fitted values. Averaging the fitted probabilities of each baby in each cell we get the green numbers above. This shows an improvement over the model with only birth weight as an explanatory variable.

Indicator Variables

toxemia = 1 if mother had toxemia
= 0 otherwise



```
. logit bpd toxemia
```

```
Iteration 0:  log likelihood = -143.06998
Iteration 1:  log likelihood = -141.64339
Iteration 2:  log likelihood = -141.63956
Iteration 3:  log likelihood = -141.63956
```

Logistic regression

Number of obs	=	223
LR chi2(1)	=	2.86
Prob > chi2	=	0.0908
Pseudo R2	=	0.0100


Log likelihood = -141.63956

bpd	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
toxemia	-.7719484	.4821775	-1.60	0.109	-1.716999 .1731021
_cons	-.5717863	.1494999	-3.82	0.000	-.8648008 -.2787718

$$\ln \left(\frac{\hat{p}_{Y|toxemia}}{1 - \hat{p}_{Y|toxemia}} \right) = -0.572 - .772 \text{ toxemia}$$

Let us look at indicator variables with logistic regression because it should remind us of something we have already seen. Recall that we looked at toxemia as an indicator variable that indicated whether the mother suffered from toxemia during the pregnancy. Here is the result of fitting a logistic regression with just toxemia as the explanatory variable.

We see that the coefficient is -0.77 and is judged not to be significant. But here is the best fitting model if we include toxemia.



$$\ln \left(\frac{\hat{p}_{Y|toxemia}}{1 - \hat{p}_{Y|toxemia}} \right) = -0.572 - .772 \text{ toxemia}$$


$$\ln \left(\frac{\hat{p}_{Y|has \text{ toxemia}}}{1 - \hat{p}_{Y|has \text{ toxemia}}} \right) = -0.572 - .772$$

$$\ln \left(\frac{\hat{p}_{Y|no \text{ toxemia}}}{1 - \hat{p}_{Y|no \text{ toxemia}}} \right) = -0.572$$

$$\ln(OR) = -.772$$

$$\Rightarrow OR = e^{-.772} = 0.46$$

So the log odds of bpd are as above. The difference between the log odds when the mother has toxemia and when the mother does not have toxemia, is the log of the odds ratio, and that is -0.772. So the odds ratio is 0.46.




. cc toxemia bpd

	Exposed	Unexposed	Total	Proportion Exposed
Cases	6	23	29	0.2069
Controls	70	124	194	0.3608
Total	76	147	223	0.3408
	Point estimate		[95% Conf. Interval]	
Odds ratio	.4621118		.1472474	1.243955 (exact)
Prev. frac. ex.	.5378882		-.2439547	.8527526 (exact)
Prev. frac. pop	.1940834			
chi2(1) = 2.66 Pr>chi2 = 0.1028				

Alternatively, we can consider the 2x2 table of bpd versus toxemia. When we analyze that table, as above, we see that the odds ratio is the same 0.462 as we got from the logistic regression analysis.

So an indicator variable and logistic regression is just another way of looking at the tables we had analyzed before. What the logistic regression approach allows us to do now is to analyze tables considering a collection of dimensions—any number of explanatory variables—together with interaction terms, etcetera.



Final model:

	coeff	Std.err.	p-value
bwt	-1.341	0.274	.0000
gestage	-0.932	0.310	.0026
toxemia	-1.359	0.624	.0293
sex	0.757	0.384	.0489
Mat. steroids	-0.921	0.425	.0302
constant	1.827	0.420	.0000

Maternal and neo-natal factors affecting bpd
based on 223 premature, small babies

Indeed, the final model for these data is above, and we see a collection of dichotomous (toxemia, sex, maternal steroids (yes/no)) and continuous explanatory variables (birth weight and gestational age). This is a much richer class of models to fit to a dichotomous response variable than is afforded by analysis as

2x2 tables. Note that the final model includes toxemia—possibly because toxemia happens later in the pregnancy and is related to gestational age.