Spider mites example

Dose of DDT	No. survived	No. dead
0.0	18	7
0.5	19	6
1.0	12	13
1.5	5	20
2.0	6	19
2.5	2	23
3.0	1	24

Binary vs. continuous outcomes

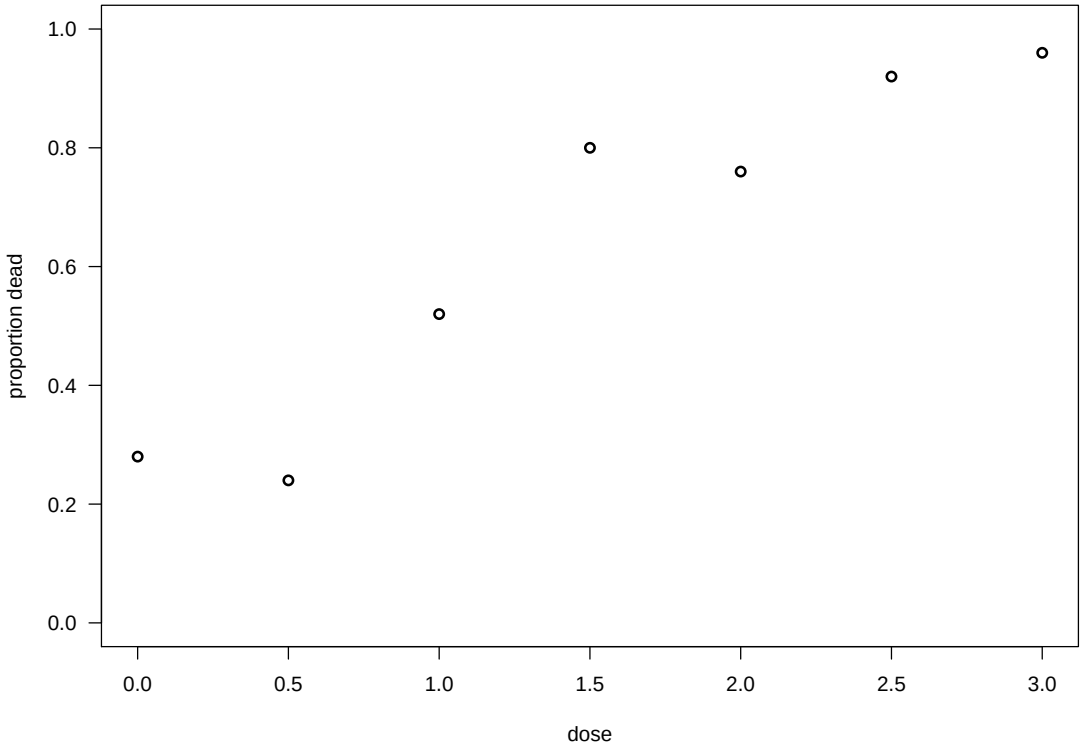
Continuous: ANOVA $\longleftrightarrow$ Regression

Binary: k $\times$ 2 table $\longleftrightarrow$?

Goals:

- Relationship between dose and Pr(dead).
- Dose at which Pr(dead) = 1/2.

A plot of the data



Linear regression

Model:

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_k x_k + \epsilon, \quad \epsilon \sim \text{ iid Normal}(0, \sigma^2)$$

This implies:

$$E(y \mid x_1, \ldots, x_k) = \beta_0 + \beta_1 x_k + \cdots + \beta_k x_k$$

β_i = increase in mean of Y associated with a unit change in x_i

Binary outcomes

Let p_d = Pr(dead | dose d)

$$p_d = \beta_0 + \beta_1 d \ ?$$

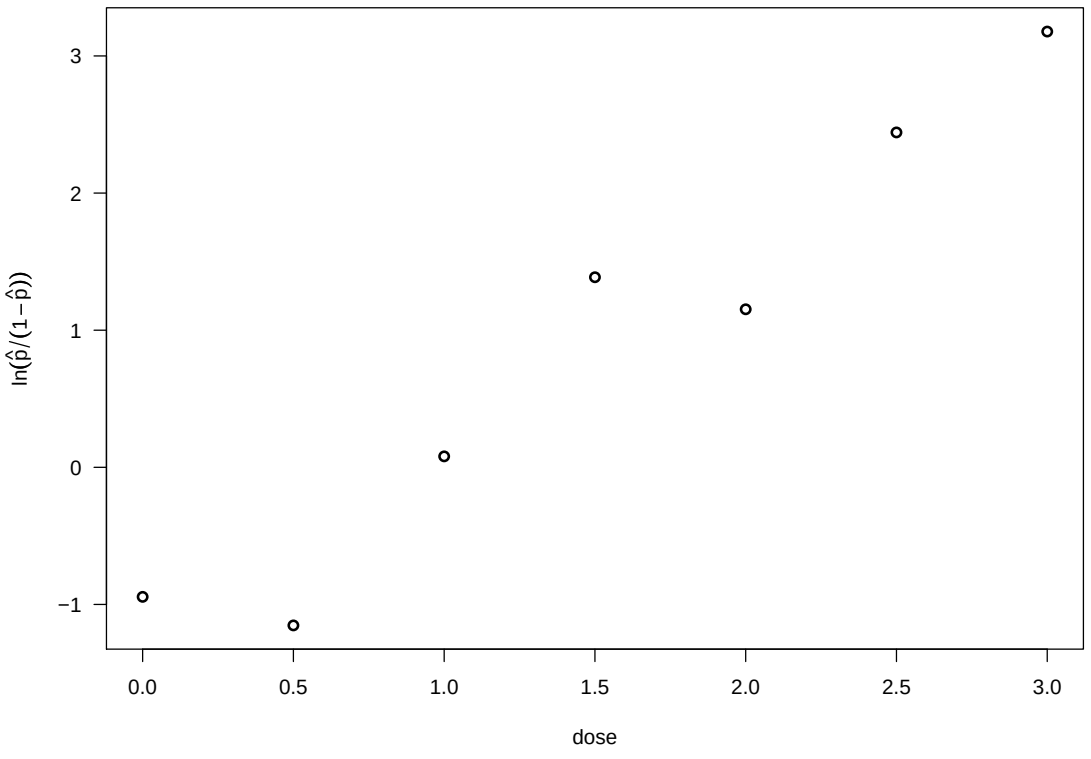
$0 \leq p_d \leq 1$ but $-\infty \leq \beta_0 + \beta_1 d \leq \infty$

Odds of death: $0 \leq \frac{p_d}{1 - p_d} \leq \infty$

log odds of death: $-\infty \leq \ln\left(\frac{p_d}{1 - p_d}\right) \leq \infty$

$\ln\left(\frac{p}{1 - p}\right)$ is also called logit(p) or the logistic function.

logit($\hat{p}_d$) vs d



Logistic regression

$$\ln\left(\frac{p_d}{1-p_d}\right) = \beta_0 + \beta_1 d$$

Try least squares, regressing $\ln\left(\frac{\hat{p}_d}{1-\hat{p}_d}\right)$ on the dose, d?

Problems:

- What if $\hat{p}_d = 0$ or 1?
- $SD(\hat{p}_d)$ is not constant with d.

Maximum likelihood

Assume $y_d \sim \text{Binomial}(n_d, p_d)$, y_d independent

with $\text{logit}(p_d) = \ln(\frac{p_d}{1-p_d}) = \beta_0 + \beta_1 d$

Note: $p_d = \dfrac{e^{\beta_0+\beta_1 d}}{1+e^{\beta_0+\beta_1 d}}$

Likelihood:

$$L(\beta_0, \beta_1 \mid y) = \prod_d p_d^{y_d} (1-p_d)^{(n_d - y_d)}$$

Logistic regression in R

Logistic regression is a special case of a "generalized linear model".

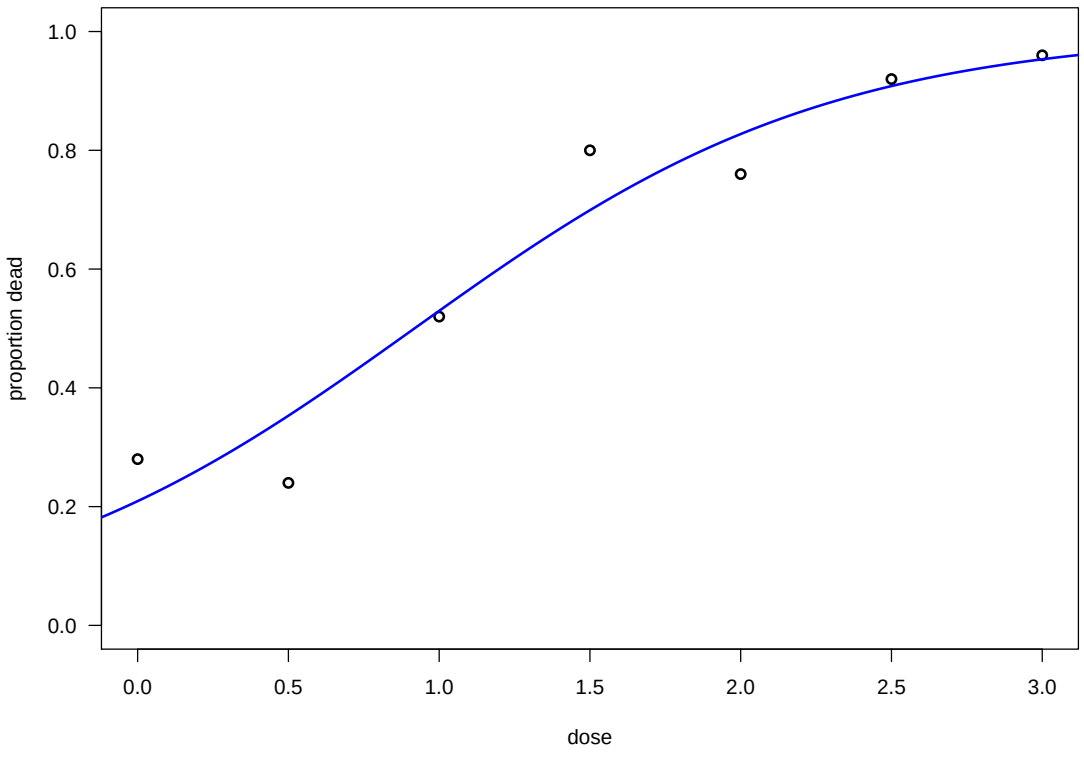
Function in R: `glm()`

```
> glm.out <- glm(n.dead/n ~ dose, weights=n, data=spiders,
                 family=binomial(link=logit))

> summary(glm.out)$coef

                 Est    SE  t-val   P-val
(Intercept)   -1.33  0.33  -4.06  <0.001
dose           1.44  0.23   6.29  <0.001
```


Fitted curve



Interpretation of β's

$$\ln\left(\frac{p_d}{1-p_d}\right) = \beta_0 + \beta_1 d$$

β_0 = log odds when dose = 0

Note: $\beta_0 = 0 \quad \longrightarrow \quad p_0 = \frac{1}{2}$

β_1 = change in log odds with unit increase in dose

Note: $\beta_1 = 0 \quad \longrightarrow$ survival unrelated to dose.

LD50

LD50 = dose at which Pr(dead | dose) = $\frac{1}{2}$.

$$\begin{aligned} \ln\left(\frac{1/2}{1-1/2}\right) &= \beta_0 + \beta_1(\text{LD50}) \\ \Longrightarrow \quad 0 &= \beta_0 + \beta_1(\text{LD50}) \\ \Longrightarrow \quad \text{LD50} &= -\beta_0/\beta_1 \end{aligned}$$

$\widehat{\text{LD50}} = -\hat{\beta}_0/\hat{\beta}_1$

$$\hat{\text{SE}}(\widehat{\text{LD50}}) \approx |\widehat{\text{LD50}}| \sqrt{\left(\frac{\hat{\text{SE}}(\hat{\beta}_0)}{\hat{\beta}_0}\right)^2 + \left(\frac{\hat{\text{SE}}(\hat{\beta}_1)}{\hat{\beta}_1}\right)^2 - 2\,\frac{\text{cov}(\hat{\beta}_0, \hat{\beta}_1)}{\hat{\beta}_0\,\hat{\beta}_1}}$$

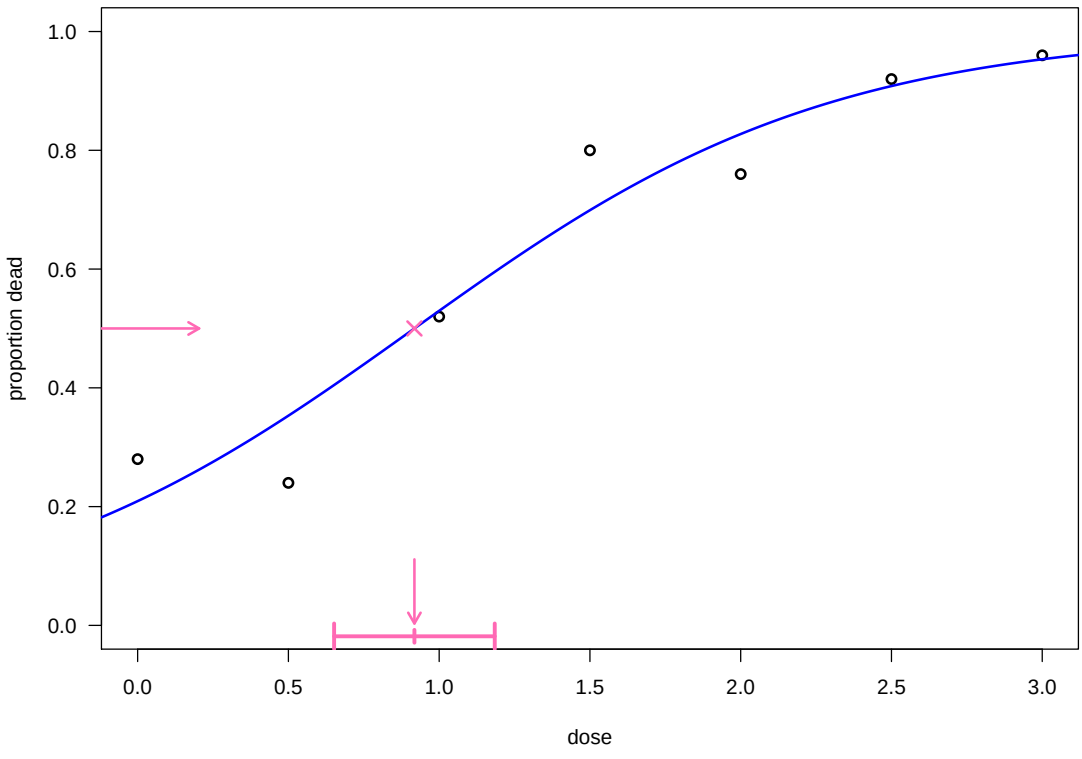
Estimating LD50 in R

```
> glm.out <- glm(n.dead/n ~ dose, weights=n, data=spiders,
                 family=binomial(link=logit))
> glm.sum <- summary(glm.out)

> co <- glm.out$coef
> ld50 <- -co[1]/co[2]
> se.co <- glm.sum$coef[,2]
> cov.co <- glm.sum$cov.scaled[1,2]
> se.ld50 <- abs(ld50) * sqrt( (se.co[1]/co[1])^2 +
                               (se.co[2]/co[2])^2 -
                               2*cov.co/(co[1]*co[2]) )

> ld50
    0.92
> se.ld50
    0.14
> ld50 + c(-1,1) * qnorm(0.975) * se.ld50
    0.65  1.18
```


LD50



Another example

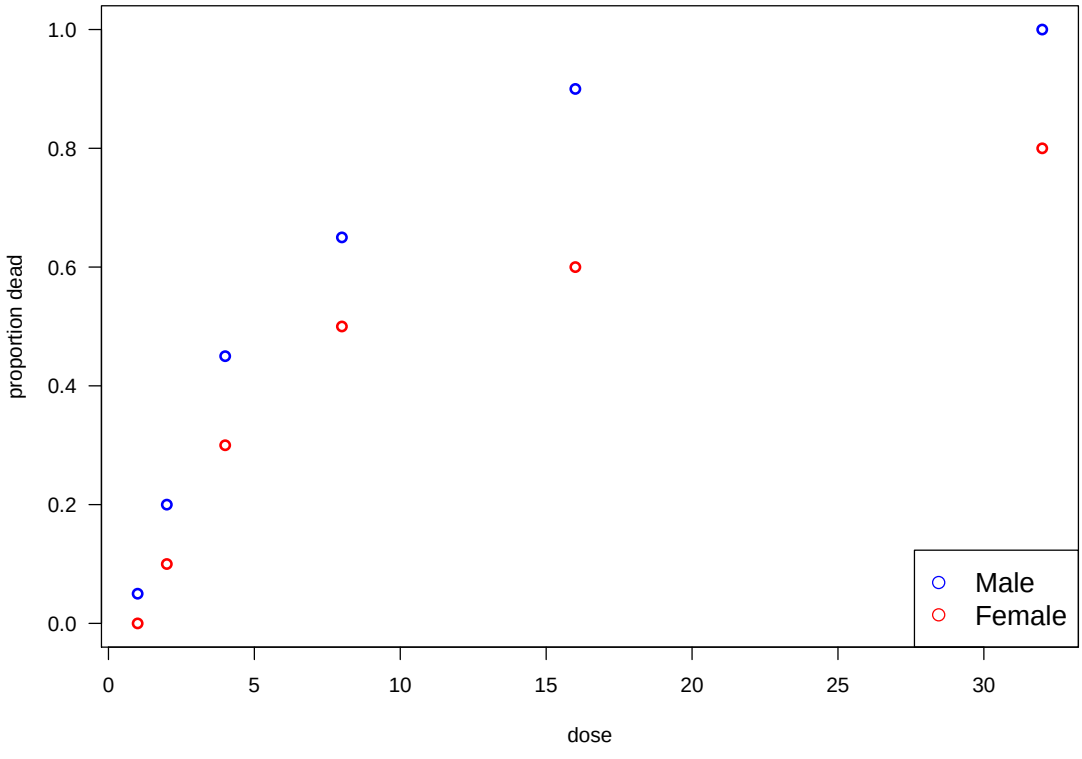
Tobacco budworm, *Heliothis virescens*

Batches of 20 male and 20 female worms were given a 3-day dose of pyrethroid *trans*-cypermethrin

The no. dead or “knocked down” in each batch was noted.

	Dose					
Sex	1	2	4	8	16	32
Male	1	4	9	13	18	20
Female	0	2	6	10	12	16

A plot of the data



Analysis in R

Assume no sex difference

```
> glm.out <- glm(n.dead/n ~ dose, weights=n, data=worms,
                 family=binomial(link=logit))

> summary(glm.out)$coef
                 Est     SE  t-val   P-val
(Intercept)   -1.57   0.23   -6.8  <0.001
dose           0.153  0.022   6.8  <0.001
```

Assume sexes completely different

```
> glm.outB <- glm(n.dead/n ~ sex*dose, weights=n, data=worms,
                  family=binomial(link=logit))

> summary(glm.outB)$coef
                  Est     SE  t-val   P-val
(Intercept)   -1.72   0.32   -5.3  <0.001
sexmale       -0.21   0.51   -0.4   0.68
dose           0.116  0.024   4.9  <0.001
sexmale:dose   0.182  0.067   2.7   0.007
```

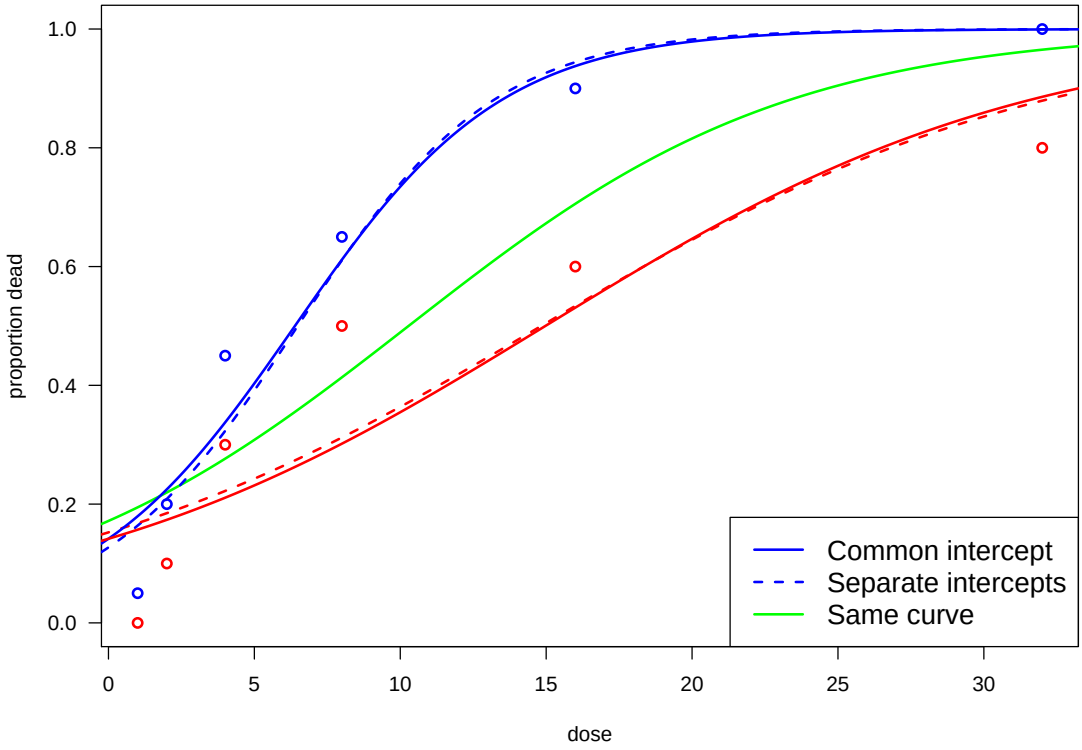

Analysis in R (continued)

Different slopes but common “intercept”

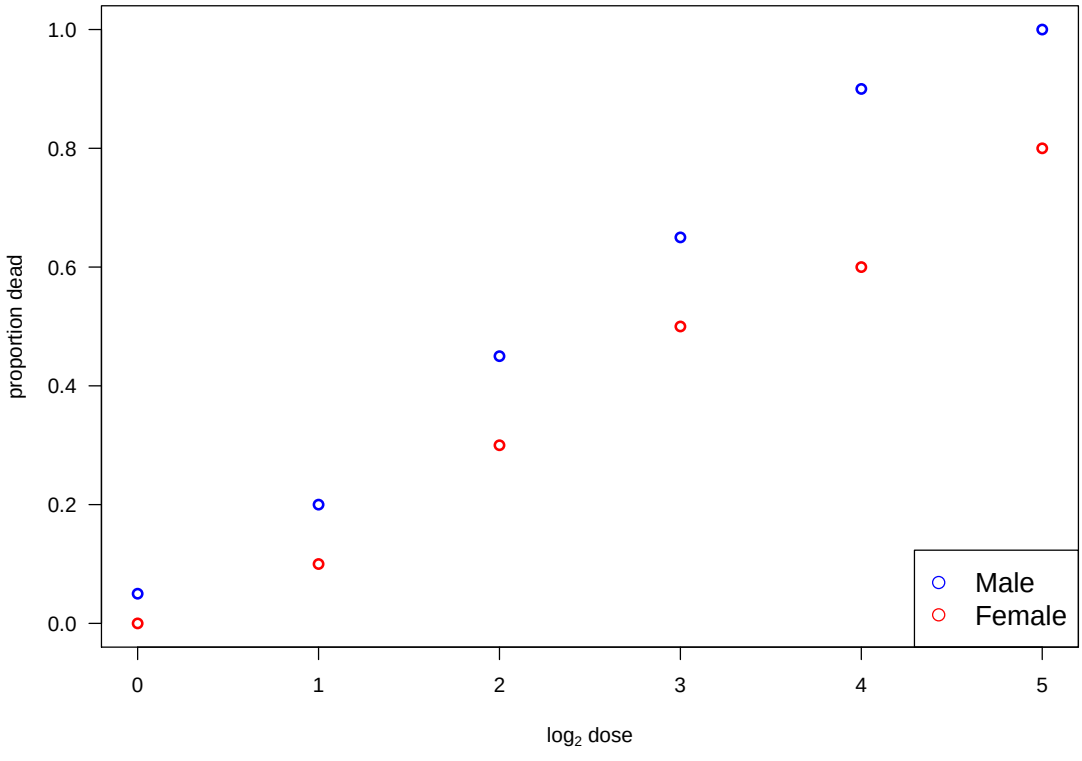
```
> glm.outC <- glm(n.dead/n ~ dose + sex:dose, weights=n,
                  data=worms, family=binomial(link=logit))

> summary(glm.out)$coef
                  Est     SE  t-val   P-val
(Intercept)   -1.80   0.25   -7.2  <0.001
dose           0.120  0.021   5.6  <0.001
dose:sexmale   0.161  0.044   3.7  <0.001
```

Fitted curves



Plot using $\log_2$ dose



Use $\log_2$ of the dose

Assume no sex difference

```
> glm.out <- glm(n.dead/n ~ dose, weights=n, data=worms,
                 family=binomial(link=logit))

> summary(glm.out)$coef
                 Est    SE  t-val   P-val
  (Intercept)  -2.77  0.37   -7.6  <0.001
  dose          1.01  0.12    8.1  <0.001
```

Assume sexes completely different

```
> glm.outB <- glm(n.dead/n ~ sex*dose, weights=n, data=worms,
                  family=binomial(link=logit))

> summary(glm.outB)$coef
                 Est    SE  t-val   P-val
  (Intercept)  -2.99  0.55   -5.4  <0.001
  sexmale       0.17  0.78   -0.2   0.82
  dose          0.91  0.17    5.4  <0.001
  sexmale:dose  0.35  0.27    1.3   0.19
```


Use $\log_2$ of the dose (continued)

Different slopes but common "intercept"

```
> glm.outC <- glm(n.dead/n ~ dose + sex:dose, weights=n,
                  data=worms, family=binomial(link=logit))

> summary(glm.out)$coef
                 Est    SE  t-val   P-val
  (Intercept)  -2.91  0.39   -7.5  <0.001
  dose          0.88  0.13    6.9  <0.001
  dose:sexmale  0.41  0.12    3.3   0.001
```

Fitted curves