Index of Lecture 4a

Practical Information

Today's session includes:

- continuation of review for logistic regression,
- continuation of prediction using `margins` command (both linear and logistic regression),
- discussion of VER model-building exercise (15, Q1-5) and this week's quiz.

Today's lecture:

- multiple logistic regression:
  - more on interpretation of coefficients,
  - statistical inference,
- new topics for logistic regression:
  - "likelihood", in particular its use for maximum likelihood estimation and likelihood-ratio tests,
  - relation to case-control studies.
- textbook (VER/MER) reading:
  16.1−8 fully covered after this lecture.

DATASET NOCARDIA (VER)

- subset of a real dataset on Nocardia mastitis in Nova Scotia dairy herds collected in 1989,
- case-control study design with 54 case and control herds,
  - 54 (all!) case herds included in study,
  - 54 non-case herds randomly selected from population of herds,
- purpose of study: evaluate the association between various exposure variables and case-control status of the herds.

Variable	Description	Values
id	farm id	(nominal)
casecont	herd status for Nocardia mastitis	0/1 (control/case)
dcpct	percent of dry cows treated	0−100 %
dneo	use of dry-cow product containing neomycin	0/1 (no/yes)
dclox	use of dry-cow product containing cloxacillin	0/1 (no/yes)
dbarn	barn type for dry cows	1=freestall 2=tiestall 3=other
numcow	number of cows milked	16−190
...	...	...

Case-Control Study and Logistic Regression

Nocardia data: outcome=`dclox`(!), explanatory=`casecont`:

	`dclox`			
`casecont`	1	0	Total	Prop. exposed
1	8	46	54	0.148
0	19	35	54	0.352
Total	27	81	108	

Statistical model:
two binomial distributions $\text{Bin}(54, p_1)$ and $\text{Bin}(54, p_0)$ for case and control populations, respectively.

Odds-ratio (OR) for comparison of exposure in case and control populations, or for comparison of risk of exposed and non-exposed herds

$$\text{OR} = \text{odds}(0.148)/\text{odds}(0.352) = 8 \cdot 35/(19 \cdot 46) = 0.320,$$

$\Rightarrow$ cloxacillin treatment protective against Nocardia mast.

Logistic regression: $\text{logit}(p_i) = \beta_0 + \beta_1 \texttt{dclox}_i$, gives:

$$\begin{aligned} \hat{\beta}_1 &= -1.138 = \ln(0.320) = \ln(\text{OR}), \\ \hat{\beta}_0 &= 0.273 \quad \leftarrow \text{meaningless for the population!} \end{aligned}$$

Same OR from 2×2-table analysis and logistic regression.[1]

[1] A statistical result states that under the assumption that the sampling proportions in case and control populations are independent of the predictors, a case-control study can be analysed by the same logistic regression model as if the design had been a cohort study, except that the estimated intercept is meaningless.

Two-way Table and Logistic Regression

Nocardia data: outcome=`dbarn`, explanatory=`casecont`:

	`dbarn`			
`casecont`	1:freestall	2:tiestall	3:other	Total
1	22	29	3	54
0	13	38	3	54
Total	35	67	6	108

Simple statistical model and analysis:
comparison of case and control populations of herds with respect to distribution of barn types $\sim \chi^2$-test.

Multiple odds-ratios by focusing only on two `dbarn` categories at a time, e.g. involving freestall barn type:

$$\text{tiestall vs. freestall}: \ \text{OR} = 13 \cdot 29/(22 \cdot 38) = 0.451,$$
$$\text{other vs. freestall}: \ \text{OR} = 13 \cdot 3/(22 \cdot 3) = 0.591.$$

Logistic regression with `dbarn` as a categorical predictor and freestall as the reference category:

$$\text{logit}(p_i) = \beta_0 + \beta_1(\texttt{dbarn}{=}2)_i + \beta_2(\texttt{dbarn}{=}3)_i,$$

gives the estimates:

$\hat{\beta}_0 = 0.526 \quad \leftarrow$ meaningless for the population!
$\hat{\beta}_1 = -0.796 = \ln(0.451) = \ln(\text{OR})$ for tiestall vs. freestall,
$\hat{\beta}_2 = -0.526 = \ln(0.591) = \ln(\text{OR})$ for other vs. freestall.

Tests of `dbarn` effect give P-values around 0.17 with both approaches (i.e., χ^2-test and logistic regression).

Odds-ratio in Multiple Logistic Regression

Basic fact:
In an additive[2] multiple logistic regression model,

$$\text{logit}(p_i) = \beta_0 + \beta_1 x_{1i} + \ldots + \beta_k x_{ki},$$

the odds-ratio for an increase of a units by predictor x_1 (say) is given by $\text{OR} = \text{e}^{\beta_1 a}$, *no matter the values of all other predictors* (as long as they are equal in the two scenarios whose probabilities we compare).

Illustration by Nocardia data and the model,

$$\begin{aligned} \text{logit}(p_i) &= \beta_0 + \beta_1 \texttt{dneo}_i + \beta_2 \texttt{dclox}_i + \beta_3 \texttt{dcpct}_i, \\ \text{logit}(\hat{p}) &= -2.98 + 2.21\,\texttt{dneo} - 1.41\,\texttt{dclox} + 0.023\,\texttt{dcpct}, \end{aligned}$$

- compare herds with $\texttt{dneo} = 1$ and $\texttt{dneo} = 0$ (i.e., $a = 1$) and any (but same!) values of other predictors,
- compute predicted probabilities on logit scale,

$$\begin{aligned} \texttt{dneo} = 1: \ \text{logit}(\hat{p}_1) &= -2.98 + 2.21 - 1.41\,\texttt{dclox} + 0.023\,\texttt{dcpct}, \\ \texttt{dneo} = 0: \ \text{logit}(\hat{p}_0) &= -2.98 + 0 - 1.41\,\texttt{dclox} + 0.023\,\texttt{dcpct}, \end{aligned}$$

- convert logit probabilities to odds,

$$\begin{aligned} \texttt{dneo} = 1: \ \text{odds}(\hat{p}_1) &= \text{e}^{-2.98+2.21-1.41\,\texttt{dclox}+0.023\,\texttt{dcpct}}, \\ &= \text{e}^{-2.98}\,\text{e}^{2.21}\,\text{e}^{-1.41\,\texttt{dclox}}\,\text{e}^{0.023\,\texttt{dcpct}}, \\ \texttt{dneo} = 0: \ \text{odds}(\hat{p}_0) &= \text{e}^{-2.98-1.41\,\texttt{dclox}+0.023\,\texttt{dcpct}}, \end{aligned}$$

- compute odds-ratio,

$$OR = \frac{\text{odds}(\hat{p}_1)}{\text{odds}(\hat{p}_0)} = \frac{\text{e}^{-2.98}\,\text{e}^{2.21}\,\text{e}^{-1.41\,\texttt{dclox}}\,\text{e}^{0.023\,\texttt{dcpct}}}{\text{e}^{-2.98}\,\text{e}^{-1.41\,\texttt{dclox}}\,\text{e}^{0.023\,\texttt{dcpct}}} = \text{e}^{2.21} = 9.14,$$

- recall that the `logistic` command always gives the OR for a one unit change (possibly inappropriate for continuous predictors).

[2] Assuming that the predictors $x_1, \ldots, x_k$ do *not* represent interaction or polynomial regression terms.

Statistical Inference for Logistic Regression

Estimation by maximum-likelihood method (next slides).[3]

Wald confidence intervals and tests:
based on estimates $\hat{\beta}_1$ (say) and standard errors $\text{SE}(\hat{\beta}_1)$:

- approximate $(1-\alpha)$ confidence interval using a standard normal reference distribution, e.g.

$$95\%\text{ CI for } \beta_1 : \ \hat{\beta}_1 \pm z^* \, \text{SE}(\hat{\beta}_1), \ z^* = 1.96 \ (z_{1-\alpha/2}),$$

- approximate z-tests of simple hypotheses, e.g. of $\text{H}_0 : \beta_1 = b$ vs. $\text{H}_a : \beta_1 \neq b$ by the z-statistic

$$z = (\hat{\beta}_1 - b)/\text{SE}(\hat{\beta}_1) \ \approx \ \text{N}(0,1) \ \text{ under } \text{H}_0,$$

- multiple Wald tests possible as well (using software),
- beware that Wald procedures do not work when either estimates or their standard errors are "extreme".[4]

Likelihood-based inference: likelihood-ratio test (next slides) and (profile) likelihood confidence interval,

- also approximate, but generally considered more precise than Wald procedures although difference often small,
- confidence intervals available in Stata using `logprof` or `pllf` add-on commands (but not core part of course).

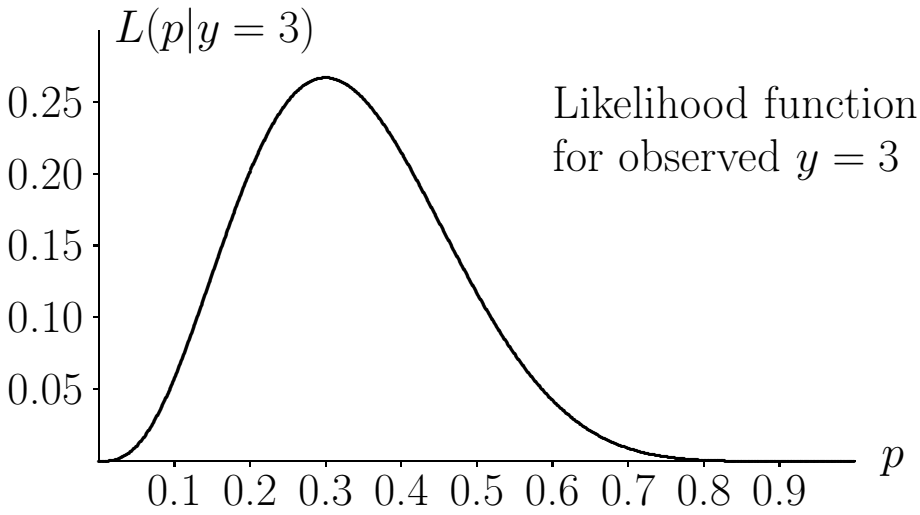
[3] Quasi-likelihood estimation is the name used for the procedure when the model contains "overdispersion" or "underdispersion" (to be discussed in a later lecture).

[4] Occurs with perfectly fitted categories, or more generally, (quasi-)separation of parameters, see e.g. Heinze & Schemper (2002), *Statist. Med.* **21**, 2409-2419.

Likelihood Function

Simple example: binomial distribution,

- consider one group of 10 mice subjected to a particular dose, and denote by
  - Y the no. of dead mice, assume we observed $Y = 3$,
  - p the probability of mice dying at this dose,
- the prob. distribution of Y is $\text{Bin}(10, p)$ with values
$$p(y) = \binom{10}{y} p^y (1-p)^{10-y}, \quad y = 0, \ldots, 10,$$
and $p(y)$ is the probability of observing y dead mice,
- the likelihood function is this function viewed as a function of the unknown parameter p and taking the observed data (y) as fixed,
$$L(p) = L(p|y) = \binom{10}{y} p^y (1-p)^{10-y}, \quad 0 \le p \le 1,$$



In general, the likelihood function is the probability (in continuous models: density value) of the observed data viewed as a function of the unknown parameters.

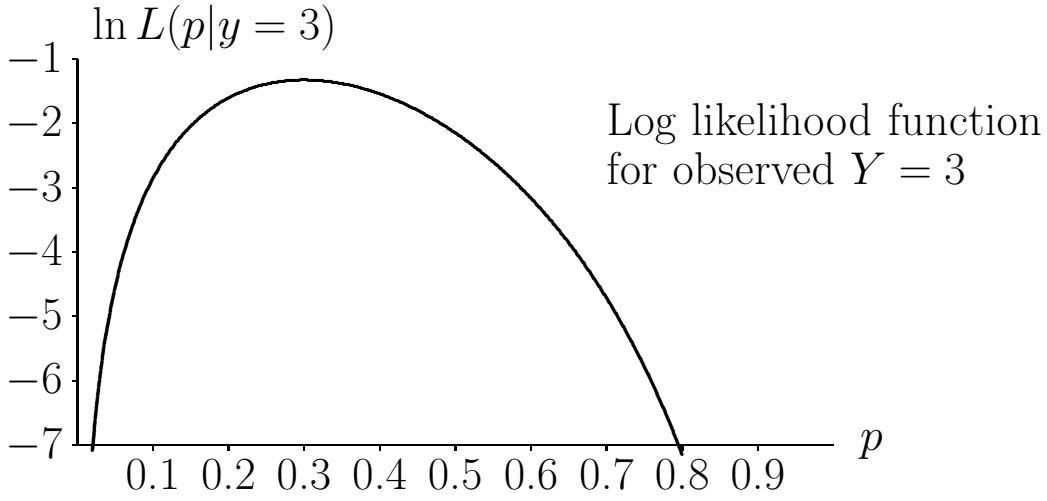
Maximum Likelihood Estimation

Idea: choose as our estimate the value of the parameter which *maximizes* the likelihood function
= the maximum likelihood estimate (MLE),

- intuitively plausible ("make the data as probable as possible"),
- general procedure applicable to all parametric models,[5]
- easy to compute analytically in many models,
- leads to estimates with good theoretical properties, in particular in large samples.

Computing the MLE in complex models (also logistic reg.):

- iterative procedure: starting value $\rightarrow$ improved value $\rightarrow$ improved value $\rightarrow \ldots \rightarrow$ no further improvement possible (convergence $\sim$ maximum found, or failure),
- convenient and common to work with $\ln L$ instead of L.



[5] In linear (regression) models, least-squares estimates are also MLEs.

Likelihood-Based Inference

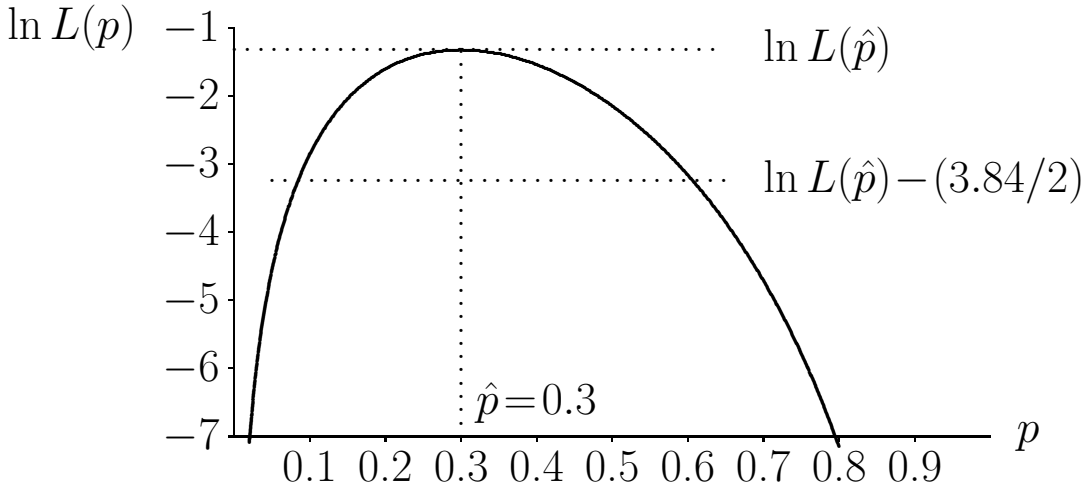
Idea: use likelihood function as our "evidence" against specific parameter values (or hypotheses),

- p's with low likelihood seem little plausible (observed data unlikely),
- p's with likelihood close to optimal seem plausible,
- statistical theory (based on large samples):
  - differences in $2 \ln L \approx \chi^2$-distribution,
  - likelihood-ratio (LR) test, denoted G^2, for comparing "full" and "reduced" model (submodel $\sim$ H_0),

    $$G^2 = 2(\ln \hat{L}_{\text{full}} - \ln \hat{L}_{\text{red}}) \approx \chi^2(\text{df}) \quad \text{under } H_0,$$

    where df = difference in no. of parameters between the models, and $\hat{L}$ = optimal likelihood values.

Example: testing $H_0 : p = p_0$ (p_0 known)



Interpretation: no evidence against p_0-values in the range $(0.08, 0.61)$ at the 5% significance level (so it's a 95% CI).

LR-tests in Logistic Regression

Example I: comparing models for `nocardia` data,

Model	$2 \ln L$	params	change prev. model G^2	df	P
`dneo,dclox,dcpct`	-107.99	4	–	–	–
`dcpct`	-138.15	2	30.16	2	<0.001
(intercept only)	-149.72	1	11.57	1	0.001

- both model reductions strongly significant,
- test against null model directly in Stata listing.

Example II: goodness-of-fit test for mice data,

Model	$2 \ln L$	params	change prev. model G^2	df	P
`dose` categorical	-117.64	12	–	–	–
`dose` continuous	-127.89	2	10.25	10	0.42

- no evidence against linear relation of dose (logit scale),
- categorical model has one "perfectly fitted category" (dose $= 0.1413$) $\Rightarrow$ care is needed in Stata.

(Technical) Deviance:
= difference in $2 \ln L$ between actual and "saturated" model,[6]

- can be used to compute G^2 for LR-test instead of $2 \ln L$,[7]
- can be used for goodness-of-fit test for grouped data if "saturated model" defined properly (not recommended[8]).

[6] "Saturated" model: one parameter for every observation or every distinct group of predictor values; different uses exist within and between softwares....

[7] In my view, there is no real advantage in using the deviance instead of $2 \ln L$.

[8] It is safer to compute the LR-test from the two model fits.

STATA DO-FILE

```
use nocardia.dta, clear
tabulate casecont dclox, chi2 row exact lrchi2
cc casecont dclox
* logistic regression for case-control design
logit casecont dclox
logit casecont dclox, or /* displays ORs */
logistic casecont dclox  /* same using logistic command */
logit dclox casecont /* to demonstrate same log(OR) */
* logistic regression for categorical predictor
tabulate casecont dbarn, chi2 row exact lrchi2
logit casecont i.dbarn
logistic casecont i.dbarn
testparm i.dbarn /* multiple Wald test for dbarn */
* multiple logistic regression
logit casecont dneo dclox dcpct
logistic casecont dneo dclox dcpct /* shows ORs */
testparm dneo /* Wald test as chi^2-test, same P as z-test */
* profile likelihood CI for dneo, using logprof add-on command
logprof dneo
* display of iterations of ML estimation
logit casecont dneo dclox dcpct, trace
* likelihood-ratio tests
logit casecont dneo dclox dcpct /* need to rerun using logit */
test dneo dclox /* Wald test for dneo+dclox */
estimates store full
logit casecont dcpct
lrtest full /* likelihood-ratio test for dneo+dclox */
lrtest full, stats /* same with all fit statistics */
estimates store red
logit casecont
estimates store null
estimates stats *
estimates table *

use mice.dta, clear
logit dead dose
estimates store red
* does not work with non-integer dose values: logit dead i.dose
egen Dose=group(dose), label /* create dose groups (in new variable Dose)  */
logit dead i.Dose /* dose as categorical predictor */
logit dead i.Dose, asis /* avoids exclusion of dose=0.1413 */
logit dead i.Dose, asis trace /* showing convergence process */
testparm i.Dose /* note: Wald test for dose fails here */
lrtest red, stats /* likelihood-ratio test ok */
```