Veterinary Epidemiology VHM 811 Course
Fall 2008, Atlantic Veterinary College, PEI
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This question for the final exam is worth 7.5% of the total course mark. It has three parts, labeled a), b), and c), that should all be answered.

The data described here were collected in the 1970'es at a veterinary university clinic. The disease studied is feline urological syndrome (or feline lower urinary tract disease) roughly characterized by the formation of crystals within the urinary bladder, leading to a range of symptoms and conditions, including bladder stones ("uroliths"). The "cause" of the disease is not completely determined, although several factors are known to affect the risk of disease.

In this study, 59 male cats brought to the clinic and diagnosed with the disease were compared to 58 cats brought to the clinic for other reasons (and therefore considered not to have the disease). The owners were asked to fill out a questionnaire detailing (among other things) information about the eating and exercising habits of the cats. We consider the following variables:

`disease`:	disease status (0=non-diseased, 1=diseased),
`sex`:	castration status (0=entire, 1=castrated),
`food`:	level of dry-food consumption (0=low, 1=high),
`exercise`:	level of exercise (0=low, 1=high).

The table below gives the counts of cats cross-tabulated by these factors:

		Sex			
		entire male		castrated male	
Exercise level	Disease category	Dry food level low	high	Dry food level low	high
low	1	2	2	3	28
	0	7	4	5	2
high	1	1	4	5	14
	0	12	11	12	5

The disease condition may be considered as "rare" in the population, and the following description can be given on possible causal pathways:

> "Thus, castration and high levels of dry cat food intake (usually associated with overfeeding) may both result in inactivity, thereby reducing blood flow to the kidneys, impairing kidney function, and therefore possibly promoting changes in the urine that are conducive to the formation of uroliths" (Thrusfield, 2007).

For simplicity, our analyses here will focus on subsets of the data involving only two of the three potential risk factors at a time. For Question a) and b) we consider the data for castrated cats only (the rightmost part of the table).

a) Describe the study design, and draw a graph to represent the causal structure between the variables involved in the dataset (for castrated cats only) you find most reasonable (prior to any data analysis). Use the graph to determine the possible epidemiological roles of the food and exercise levels on the disease status; e.g., whether the food level could be a confounder for the effect of exercise on disease, or the exercise level could be a confounder for the effect of food on disease, or other roles.

b) Use the data in the table and any of the attached Stata listings to carry out an epidemiological analysis to determine the actual roles of the two variables (in the dataset for castrated cats only). Summarize the relations between the variables with suitable measures of association. If you would like to compute additional measures (not present in the Stata listing), you may either compute them manually (for calculations that are not too complex) or give the relevant Stata command(s) to compute them.

c) These data have been used in several textbooks of veterinary epidemiology to illustrate interaction (Martin *et al.*, 1987; Thrusfield, 2007). We will reconstruct the calculations and reasoning leading to the determination of an interaction. For this part, we consider the data for cats subjected to a high level of exercise (the bottom rows of the table). The VER text states that two factors exhibit an *additive* interaction if the risk differences relative to the reference cell (0,0) for the two factors fail to satisfy the additive equation,

$$\mathrm{RD}_{11} = \mathrm{RD}_{01} + \mathrm{RD}_{10}. \tag{1}$$

It can be shown that Equation (1) is mathematically equivalent to the following equation expressed in terms of the risk ratios relative to the same cell,

$$\mathrm{RR}_{11} = \mathrm{RR}_{01} + \mathrm{RR}_{10} - 1. \tag{2}$$

Use this equation as well as the data in the table and any of the attached Stata listings, to give assessments of whether the data (for high level exercise cats) exhibit an additive or multiplicative interaction (or both) between food and sex. State also the direction of any interaction you find.

Stata listing (full dataset)

```
. list sex disease food exercise n, separator(8)

     +-------------------------------------+
     | sex   disease   food   exercise    n |
     |-------------------------------------|
  1. |   0         1      0          0    2 |
  2. |   0         0      0          0    7 |
  3. |   0         1      0          1    1 |
  4. |   0         0      0          1   12 |
  5. |   0         1      1          0    2 |
  6. |   0         0      1          0    4 |
  7. |   0         1      1          1    4 |
  8. |   0         0      1          1   11 |
```

```
     +-------------------------------------+
     | sex   disease   food   exercise    n |
     |-------------------------------------|
  9. |   1         1      0          0    3 |
 10. |   1         0      0          0    5 |
 11. |   1         1      0          1    5 |
 12. |   1         0      0          1   12 |
 13. |   1         1      1          0   28 |
 14. |   1         0      1          0    2 |
 15. |   1         1      1          1   14 |
 16. |   1         0      1          1    5 |
     +-------------------------------------+
```

Stata listing for part b):

```
. cs disease food [fw=n] if sex==1, by(exercise) or

        exercise |       OR       [95% Conf. Interval]   M-H Weight
-----------------+-------------------------------------------------
               0 |    23.33333     3.424559   158.7685     .1578947 (Cornfield)
               1 |        6.72     1.609697   28.05491     .6944444 (Cornfield)
-----------------+-------------------------------------------------
           Crude |       12.75     4.065908   40.01652
    M-H combined |    9.797599     3.002393   31.97215
-----------------------------------------------------------------------
Test of homogeneity (M-H)      chi2(1) =    0.961  Pr>chi2 = 0.3270

                   Test that combined OR = 1:
                               Mantel-Haenszel chi2(1) =     17.17
                                                Pr>chi2 =    0.0000
. cs disease exercise [fw=n] if sex==1, by(food) or

            food |       OR       [95% Conf. Interval]   M-H Weight
-----------------+-------------------------------------------------
               0 |    .6944444     .1262066   3.687623         1.44 (Cornfield)
               1 |          .2            0   1.033649     2.857143 (Cornfield)
-----------------+-------------------------------------------------
           Crude |    .2523719     .0903142   .7086057
    M-H combined |    .3656915     .1094318   1.222042
-----------------------------------------------------------------------
Test of homogeneity (M-H)      chi2(1) =    0.955  Pr>chi2 = 0.3285

                   Test that combined OR = 1:
                               Mantel-Haenszel chi2(1) =      2.76
                                                Pr>chi2 =    0.0964
```

Stata listing for part c):

```
. cs disease sex [fw=n] if exercise==1, by(food) or

            food |       OR       [95% Conf. Interval]   M-H Weight
-----------------+-------------------------------------------------
               0 |          5     .6360854           .            .4 (Cornfield)
               1 |        7.7     1.722763   34.35628     .5882353 (Cornfield)
-----------------+-------------------------------------------------
           Crude |    5.141176     1.639108    15.9506
    M-H combined |    6.607143     1.822118   23.95802
-----------------------------------------------------------------------
Test of homogeneity (M-H)      chi2(1) =    0.095  Pr>chi2 = 0.7578

                   Test that combined OR = 1:
                               Mantel-Haenszel chi2(1) =      9.11
                                                Pr>chi2 =    0.0025

. cs disease food [fw=n] if exercise==1, by(sex) or

             sex |       OR       [95% Conf. Interval]   M-H Weight
-----------------+-------------------------------------------------
               0 |    4.363636     .5361895           .     .3928571 (Cornfield)
               1 |        6.72     1.609697   28.05491     .6944444 (Cornfield)
-----------------+-------------------------------------------------
           Crude |         4.5     1.497335   13.42886
    M-H combined |    5.868613     1.686171   20.42534
-----------------------------------------------------------------------
Test of homogeneity (M-H)      chi2(1) =    0.095  Pr>chi2 = 0.7582

                   Test that combined OR = 1:
                               Mantel-Haenszel chi2(1) =      8.34
                                                Pr>chi2 =    0.0039
```