Lab 5 - Instructor Guide

Relating Risk Factors to Health

Goals: calculate and understand epidemiologic measures of association and impact

Background

Several well-designed and executed epidemiologic studies have implicated enviroxide as a potential cause of environitis, a newly recognized disorder in a small country called Carolina (pop. 10,000). In addition, a hitherto-unseen form of influenza, influenza J, has also been discovered and is believed to be associated with exposure to birds as household pets. Although they are unrelated, the two disorders have similar clinical pictures, with a two-week acute phase for which the most prominent symptom is a profound feeling "like being back in graduate school". Fortunately symptoms resolve quickly and completely, with apparent immunity to further episodes. Recent survey data indicates that 15% of the population are exposed to high levels (>100ppm) of enviroxide; 40% of the population have a pet bird in the household. There is no association between these two exposures.

Separate research teams conduct two-year cohort studies of these disorders. Thanks to Carolina's very low mortality rate and restrictive emigration policies, there is no loss to follow-up in either study. The first study recruits 1,000 persons living in buildings with enviroxide levels>100ppm ("exposed") and 1,000 persons living in buildings with enviroxide levels ≤100ppm ("unexposed"); 700 exposed participants develop environitis, as do 500 unexposed participants. In the second study 2,000 bird owners ("exposed") and 2,000 persons who do have any contact with birds ("unexposed") are recruited; 400 exposed participants contract influenza J; 160 unexposed participants do also.

Questions

Part A. Measures of association

1. Create a 2 x 2 table for each cohort study.

	Study 1: Environitis			Study 2: Influenza J		
	Enviroxide	Unexposed	Total	Pet birds	Unexposed	Total
Cases	700	500	1,200	400	160	560
Noncases	300	500	800	1,600	1,840	3,440
Total	1,000	1,000	2,000	2,000	2,000	4,000

2. For each study calculate the following measures. For rate computations, assume that cases occurred uniformly during the follow-up period.

   a. incidence proportions (cumulative incidences, CI)

   b. incidence rates (incidence densities, ID)

c. cumulative incidence ratios (CIR)

d. incidence density ratios (IDR)

e. odds ratios (OR)

f. risk differences (cumulative incidence differences, CID)

g. incidence rate differences (incidence density differences, IDD).

	Study 1			Study 2		
	Enviroxide	**Unexposed**	**Total**	**Pet birds**	**Unexposed**	**Total**
a) CI*:	**0.70**	**0.50**	**0.60**	**0.20**	**0.08**	**0.14**
b) ID:	**0.54/y**	**0.33/y**	**0.43/y**	**0.11/y**	**0.04/y**	
						0.075/y
c) CIR*:		**1.4**			**2.5**	
d) IDR:		**1.6**			**2.6**	
e) OR*:		**2.3**			**2.9**	
f) CID*:		**0.20**			**0.12**	
g) IDD:		**0.21/y**			**0.07/y**	

*** Over two years (note that in study 2, where incidences are much lower than in study 1, the ID is about half of the two-year CI).**

3. Compare and contrast the ratio measures in each cohort, why do differences exist?

Since influenza J has a lower incidence than does Environitis, the CIR, IDR, and OR are more alike for influenza J than is the case for environitis. For the latter, the OR is quite different from the CIR. For more explanation, please see the FAQ "I don't understand the odds ratio" (http://www.sph.unc.edu/courses/epid168/public/faq.html).

Part B. Measures of impact – adverse exposures

1. For which associations do the data provide stronger evidence that the association is causal?

Comparison of the CIR's or the IDR's for the two associations shows a stronger association (based on the ratio measure) for the pet bird/influenza J association, thus providing stronger evidence that the relationship is causal.

2. In preparation for the next election, the Carolina government is seeking a public health success. Assuming that resources and intervention expertise are available to eliminate either enviroxide or pet birds, but not both, which of these two exposures should be chosen for the prevention program in order to have the most visible results? What epidemiologic measure(s) can assist you in this decision?

   First, we need to consult with the government's political advisors regarding what will be most salient to the media and the public, i.e., what determines "visibility". One factor might be the reduction in the actual number of cases of the disease ("new government program averts 5,000 cases of environitis"). Another might be the proportionate reduction risk of disease ("influenza J cut by 40%, claims government health expert"). Presumably the indicator chosen will depend upon the prevalence of exposure in the population as well as the relative risk.

   Once we have established what parameters are most salient, then we must choose the appropriate epidemiologic measure, presumably a population attributable risk measure. Note that the two cohort studies were designed to have equal numbers of exposed and unexposed participants, to maximize statistical power, but the population prevalences (see second paragraph) are quite different (15% for high enviroxide, 40% for pet bird ownership). Since the strength of association and exposure prevalence are both greater for influenza J and pet bird ownership, the latter is the recommended target for intervention.

   If the political advisors want to have the information in terms of absolute number of cases, then the population attributable risk (PAR) multiplied by the size of the population at risk (exposed plus unexposed) provides the answer. If a proportional measure is desired, then the population attributable risk percent (PARP) will give the answer.

	Environitis			**Influenza J**		
	Enviroxide	**Unexposed**	**Total**	**Pet birds**	**Unexposed**	**Total**
Pop at risk	**1,500**	**8,500**	**10,000**	**4,000**	**6,000**	**10,000**
CI (from above)	**0.7**	**0.5**		**0.20**	**0.08**	
Total cases	**1,050**	**4,250**	**5,300**	**800**	**480**	**1,280**

	Environitis	**Influenza J**
PAR	**CID x P_1 = 0.20 x 0.15 = 0.03**	**CID x P_1 = 0.12 x 0.40 = 0.048**
Cases averted	**0.03 x 10,000 = 300**	**0.048 x 10,000 = 480**

PARP*

$$\frac{0.15(1.4-1)}{1 + 0.15(1.4-1)} = 5.7\% \qquad \frac{0.40(2.5-1)}{1 + 0.40(2.5-1)} = 37.5\%$$

***Formula:**

$$\frac{P_1(\mathrm{CIR}-1)}{1 + P_1(\mathrm{CIR}-1)}$$

Part C. Measures of impact – preventive exposure

Eliminating pet bird ownership will not be popular, however. Seeking a biomedical solution, the government launches a crash program to develop a vaccine. In the subsequent double-blind, randomized efficacy trial of the candidate vaccine, among 162 persons receiving the vaccine 9 subsequently develop influenza J; of the 169 receiving placebo, 24 contract influenza J.

1. What is the efficacy of the new vaccine? (i.e. in what percent of the study group was disease prevented?)

$$\textbf{vaccine: } CI_1 = 9 / 162 = 0.056$$
$$\textbf{placebo: } CI_0 = 24 / 169 = 0.142$$

$$PF_1 = \frac{0.142 - 0.056}{0.142} = 0.606 \approx 61\%$$

2. Focus groups suggest that only 30% of the population will accept the vaccine, however. If this projection is correct, what will the population effectiveness of the vaccine be?

PF = 0.3 x .606 = 18.2%

3. Given the low effectiveness due to the behavioral aspect of vaccine administration, Carolina public health strategists opt instead for environmental modification and preventing environitis. They propose a crash enviroxide abatement program to completely eliminate enviroxide exposure. What proportion of environitis cases will be prevented?

   a. In persons living in buildings with enviroxide?

$$ARP = CI_1 - CI_0)/CI_1 = (.7 - .5)/.7 = .286 \text{ or } 28.6\%$$
$$\text{or } ARP = (RR - 1)/RR = (1.4 - 1)/1.4 = 28.6\%$$

   b. In the population:

$$PARP = \frac{P_1(RR-1)}{1 + P_1(RR-1)} \quad \frac{(.15)\ (1.4-1)}{1+(.15)\ (1.4-1)} = .057 \text{ or } 5.7\%$$

Part D. Interpretation of odds ratios

Suppose a case-control study examining influenza J and pet bird ownership found an OR=3.0. At the end of the flu season, all reported influenza J cases are interviewed and compared with persons chosen from a sample of all others in the population. Examine the following statements and comment on why the statement correctly or incorrectly reflects the meaning of the above odds ratio.

1. The odds of developing Influenza J for a pet bird owner are 3 times higher than those for a person who does not have contact with birds.

    Although risk of disease (and, equivalently, odds of disease) cannot be directly estimated from data on cases and controls only, the odds ratio computed from exposure odds is algebraically equivalent to the odds ratio based on disease odds. For that reason this statement correctly interprets the above odds ratio.

2. The risk of developing influenza J in pet bird owners is 3 times that of developing influenza J in nonowners.

    This statement translates the odds ratio into a risk ratio. Although a risk ratio (or CIR) cannot be directly estimated from a case-control study such as the above, the odds ratio does approximate the risk ratio when disease incidence is low (i.e., a "rare" disease). The incidence of influenza J is not really "rare" (14% of exposed, 8% of unexposed). so this translation overstates the amount of the actual risk ratio. However, since the incidences are of modest size, the overestimation is also small.

3. The odds of bird ownership among persons who contract influenza J are 3 times those for persons who do not contract influenza J.

    This is a literal translation of the odds ratio estimated in the above-described case-control study, since it is phrased in terms of odds of exposure. Exposure prevalence, and therefore exposure odds, can be directly estimated in a case-control study, since cases and controls are recruited and then interviewed. Although correct and precise, however, this translation is not as meaningful as the previous ones since our real interest is risk of disease, rather than prevalence of exposure.