Exercise - measures of association

Mycoplasma in Californian dairies

In a study of mycoplasma-mastitis in Californian dairy herds a group of problem herds were identified by laboratory microbiological growth tests using bulk tank milk samples. Positive herds were grouped on the basis of number of mycoplasma colonies on agar plates from laboratory tests (<= 50 colonies and > 50 colonies). A group of control herds was chosen among the herds that showed no colonies at the laboratory test. The laboratory results were combined with extra information obtained from the Dairy Herd Improvement Association on herd size and annual culling percent. Herds were grouped as shown in the following table:

		Infection status		
		Cases		Controls
Exposure level		<= 50 colonies	> 50 colonies	
Herd size	< 350 350 - 699 >= 700	6 12 5	2 13 5	45 25 4
Annual culling percent	< 29% >= 29%	8 15	4 16	34 43

- What type of study design has been used?
- Given the study design, which measure of association would be appropriate?
- Calculate the measure of association between herd size and infection status and between annual culling percent and infection status.

Answer

This is a case-control study, because cases and controls were separately sampled among infected and non-infected herds. Because we have a case control design, the appropriate measure of association is the odds ratio. Association between herd size and infection status:

	Case	Control	Total
Size >=350	35	29	64
Size < 350	8	45	53
Total	43	74	117

```
library(epiR)
epi.2by2(a = 35, b = 29, c = 8, d = 45, method = "case.control", conf.level = 0.95,
verbose = FALSE)
```

Large herds (greater than 350 cows) had 6.79 (95% confidence interval 2.76 -- 16.68) times the odds of mycoplasma infection, compared with small herds (less than 350 cows). What is the association between annual cull rate and infection status?

	Case	Control	Total
Cull >=29%	31	43	74
Cull < 29%	12	34	46
Total	43	77	117

```
epi.2by2(a = 31, b = 43, c = 12, d = 34, method = "case.control", conf.level = 0.95,
verbose = FALSE)
```

High cull-rate herds (annual cull rate greater than 29%) had 2.04 (95% confidence interval 0.91 -- 4.56) times the odds of mycoplasma infection, compared with low cull-rate herds (those with an annual cull rate of less than 29%).

Calf scours

At the investigation of a diarrhoea outbreak in a calf herd, faecal samples from 14 randomly selected calves with diarrhoea and from 14 randomly selected calves without diarrhoea were sent for laboratory investigation. The results

show that 8 of the 14 calves with diarrhoea were infected with pathogenic E.coli bacteria, and 5 of the 14 calves without diarrhoea were infected with pathogenic E.coli.

- Which design has been used?
- What proportion of diarrhoea among E.coli infected calves is due to infection with pathogenic E.coli?
- What proportion of diarrhoea in the whole herd is due to infection with pathogenic E.coli?

Answer

This is a case-control design because the calves were sampled separately among cases and non-cases. Because we are using a case-control design, the relevant measure of association is the odds ratio. The proportion of diarrhoea among E.coli infected calves due to infection with pathogenic E.coli is calculated as the estimated attributable fraction (AF). First construct a 2 × 2 table:

	Diseased	**Non-diseased**	**Total**
E.coli present	8	5	13
E.coli absent	6	9	15
Total	14	14	28

```
library(epiR)
epi.2by2(a = 8, b = 5, c = 6, d = 9, method = "case.control", conf.level = 0.95,
verbose = FALSE)
```

The odds for the presence of infection with E.coli is 2.4 times higher among diarrhoea calves than among non-diarrhoea calves. We may say that odds of diarrhoea is 2.4 (95% CI 0.52 - 11) times higher among pathogenic E.coli infected calves than among non-infected calves.

This result is used to estimate the proportion of diarrhoea among E.coli infected calves which is due to infection with E.coli (the estimated attributable fraction). The estimated attributable fraction is 0.58 (95% CI -0.91 -- 0.91). This means that 58% of diarrhoea cases among E.coli infected calves is due to infection with E.coli.

The proportion of diarrhoea in the whole herd due to E.coli (in the case of a case control study) is the estimated population attributable fraction. The estimated population attributable fraction is 0.33 (95% confidence interval -0.52 -- 0.52). This means that 33% of the cases of diarrhoea in the herd is due to the fact that some calves are infected with pathogenic E.coli bacteria. If we could prevent infection with pathogenic E.coli in the herd, we could reduce the occurrence of diarrhoea 33%. This also means that 67% of diarrhoea cases in the herd are due to other reasons than infection with pathogenic E.coli. In the above calculations it is assumed to be 100% sensitive and 100% specific.

Thyroid problems

Of 2,872 individuals who had received radiation treatment in childhood because of an enlarged thymus, 24 developed cancer of the thyroid and 52 developed benign thyroid tumours. A comparison group consisted of 5,055 children who received no such treatment (brothers and sisters of those who received radiation treatment). During the follow-up period none of the comparison group developed thyroid cancer, but six developed benign thyroid tumours. Calculate: (1) the relative risk of thyroid cancer, (2) the relative risk of benign thyroid tumours. Describe the results in your own words.

Answer

	Diseased	**Non-diseased**	**Total**
Exposed	24	2848	2872
Non-exposed	0	5055	5055
Total	24	7903	7927

The relative risk for cancer of the thyroid cannot be estimated in a meaningful way since the comparison group was too small (and/or the follow-up time too short for anyone to fall ill). There is, however, an appreciable difference between the exposed and non-exposed groups (24 out of 2832 is considerably more than 0 out of 5055). Compute the relative risk of benign thyroid tumours:

	Diseased	Non-diseased	Total
Exposed	52	2820	2872
Non-exposed	6	5049	5055
Total	58	7869	7927

```
library(epiR)
epi.2by2(a = 52, b = 2820, c = 6, d = 5049, method = "cohort.count", conf.level =
0.95, verbose = FALSE)
```

Benign thyroid tumours were 15 times (95% confidence interval 12 -- 20) common in the exposed group, compared with the non-exposed group.

Cholesterol and blood pressure

In a screening program, 1329 men aged 40 - 59 years had their serum cholesterol and systolic blood pressure measured. They were then followed over a 6-year period for the development of coronary heart disease. At the beginning of the period all were free of coronary heart disease. For the data presented below, calculate the relative risk of coronary heart disease in relation to men with serum cholesterol under 220 mg/100mL and systolic blood pressure under 147 mm Hg for:

- Men with serum cholesterol 260 mg/100mL and higher and systolic blood pressure under 147 mm Hg.
- Men with serum cholesterol under 220 mg/100mL and higher and systolic blood pressure 167 mm Hg and higher.
- Men with serum cholesterol 260 mg/100mL and higher and systolic blood pressure 167 mm Hg and higher.

	Systolic blood pressure [a]					
	< 147		147 - 166		> 166	
Serum cholesterol [b]	**n**	**CHD**	**n**	**CHD**	**n**	**CHD**
< 220	431	10	93	3	49	7
220 - 259	347	19	74	6	49	6
> 259	185	19	57	11	44	11

[a] mm Hg
[b] mg/100mL

Answer

The relative risk of coronary heart disease for men with serum cholesterol 260 mg/100mL and higher and systolic blood pressure under 147 mm Hg, compared with those with serum cholesterol under 220 mg/100mL and systolic blood pressure under 147 mm Hg:

	Diseased	Non-diseased	Total
Chol >259; BP <147	19	166	185
Chol <220; BP <147	10	421	431
Total	29	587	616

```
library(epiR)
epi.2by2(a = 19, b = 166, c = 10, d = 421, method = "cohort.count", conf.level =
0.95, verbose = FALSE)
```

Men with serum cholesterol 260 mg/100mL and higher and systolic blood pressure under 147 mm Hg had 4.43 (95% confidence interval 2.84 -- 6.89) times the risk of coronary heart disease, compared with those with serum cholesterol under 220 mg/100mL and systolic blood pressure under 147 mm Hg.

The relative risk of coronary heart disease for men with serum cholesterol less than 220 mg/100mL and systolic blood pressure greater than 166 mm Hg, compared with those with serum cholesterol under 220 mg/100mL and systolic blood pressure under 147 mm Hg:

	Diseased	Non-diseased	Total

Chol <220; BP >166	7	42	49
Chol <220; BP <147	10	421	431
Total	17	463	480

```
epi.2by2(a = 7, b = 42, c = 10, d = 421, method = "cohort.count", conf.level = 0.95,
verbose = FALSE)
```

Men with serum cholesterol under 220 mg/100mL and systolic blood pressure greater than 166 mm Hg had 6.16 (95% confidence interval 2.93 -- 12.95) times the risk of coronary heart disease, compared with those with serum cholesterol under 220 mg/100mL and systolic blood pressure under 147 mm Hg.

The relative risk of coronary heart disease for men with serum cholesterol greater than 259 mg/100mL and systolic blood pressure greater than 166 mm Hg, compared with those with serum cholesterol under 220 mg/100mL and systolic blood pressure under 147 mm Hg:

	Diseased	**Non-diseased**	**Total**
Chol >259; BP >166	11	33	44
Chol <220; BP <147	10	421	431
Total	21	454	475

```
epi.2by2(a = 11, b = 33, c = 10, d = 421, method = "cohort.count", conf.level =
0.95, verbose = FALSE)
```

Men with serum cholesterol greater than 259 mg/100mL and systolic blood pressure greater than 166 mm Hg had 10.78 (95% confidence interval 5.87 -- 19.79) times the risk of coronary heart disease, compared with those with serum cholesterol under 220 mg/100mL and systolic blood pressure under 147 mm Hg.

Influenza

An influenza vaccine was tested on a voluntary group of young female student nurses. Of the 95 individuals who received the vaccine, 3 fell ill and of the 48 who received a placebo, 8 fell ill with influenza during the follow-up period. Moderate or marked discomfort after vaccination was reported by 27% of those who received vaccine and by 24% of those who received the placebo. Calculate the relative risk of: (1) contracting influenza, and (2) experiencing discomfort after treatment. Describe the results in your own words.

Answer

The relative risk of contracting influenza after vaccination:

	Influenza +	**Influenza +**	**Total**
Vacc +	3	92	95
Vacc -	8	40	48
Total	11	132	143

```
library(epiR)
epi.2by2(a = 3, b = 92, c = 8, d = 40, method = "cohort.count", conf.level = 0.95,
verbose = FALSE)
```

Vaccinated nurses had 0.19 (95% confidence interval 0.06 -- 0.57) times the risk of contracting influenza, compared with non-vaccinated nurses. The relative risk of discomfort after treatment:

	Discomfort +	**Discomfort +**	**Total**
Vacc +	26	69	95
Vacc -	12	36	48
Total	38	105	143

```
epi.2by2(a = 26, b = 69, c = 12, d = 36, method = "cohort.count", conf.level = 0.95,
verbose = FALSE)
```

Vaccinated nurses had 1.09 (95% confidence interval 0.82 -- 1.46) times the risk of discomfort after treatment, compared with non-vaccinated nurses. The occurrence of influenza among the vaccinated group was about 20% that of the placebo group (that is, a decrease of 80%). The occurrence of discomfort after treatment was about 10% higher among those that received the vaccine.