

## UNIT 6 ESTIMATION AND CONFIDENCE INTERVALS

### AIMS

The aims of this session are to:

- Re-iterate the ideas of statistical inference - in particular estimation.
- Explore the concept of confidence interval estimation.

### OBJECTIVES

At the end of Unit 6 you should be able to:

- Explain the process of statistical inference and the idea of estimation in particular.
- Show, with a numeric example, that you understand the idea of a confidence interval.
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- Interpret the meaning of a specific confidence interval for the population mean, proportion and median, and for the differences between two such measures.
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- Explain with a numeric example the idea of a confidence interval for a ratio.
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- Interpret confidence intervals for risk and odds ratios.

Reading: Review the discussion of statistical inference at the start of Week 1.  
Bland: Chapter 7.  
or Bowers-2: pp. 7-22; 25-30; 38-47.

## Introduction

We saw in Unit 1 that if we want to determine the value of some population parameter, we can take a representative sample calculate the appropriate sample statistic, and use this value as the basis for an estimate of the true (population) parameter value. This is what we mean by estimation.

Suppose we wanted to estimate the mean systolic blood pressure of all male police officers in West Yorkshire (the population), and a sample of 500 officers gives a sample mean systolic blood pressure of 135mmHg (the sample statistic). Then we would estimate the true (population) systolic blood pressure to be about 135mmHg. We say "about" because no sample, even a random sample, is going to be exactly the same as the population from which it is taken. So we have to allow for a little uncertainty. We'll see how we do this shortly.

There is an alternative approach, known as *hypothesis testing*. The appropriate sample statistic is compared with the hypothesised value to see if it provides sufficient evidence for the latter to be substantiated or not.

## Confidence intervals

Knowing that the sample mean in the hypothetical systolic blood pressure example above is 135mmHg tells us that the true (population) mean is also *about* 135mmHg. The "about" is to allow for uncertainty caused by unavoidable differences between any sample and its parent population.

Helpfully, there is a way to take this uncertainty into account. We can calculate a *range* of values known as a **confidence interval**, within which we can be 95% confident that the true population mean value will be found. The value of 95% is known as the **confidence level**. Confidence intervals providing a level of confidence of 99% can also be calculated (you will not be expected to be able to calculate any sort of confidence interval).

For example, suppose the 95% confidence interval for the true (population) mean systolic blood pressure is found to be:

(120 to 150) mmHg.

This result means that we can be 95% confident that the true (and unknown) population mean systolic blood pressure is somewhere between 120 and 150mmHg. A confidence interval is said to represent a **plausible range** of

values for the true (population) mean (or proportion or median, or whatever parameter is being estimated).

An alternative interpretation is that if we were to take say 100 same-size samples from this population and calculate the 95% confidence interval for the true mean for each sample, then we can expect that 95 of the confidence intervals actually will contain the true population mean value. Unhappily however 5 of the samples will not. The trouble is, we never know whether our single sample is one of the 95 which does contain the true mean or one of the 5 which doesn't. But we take comfort from the fact that 95% of the time it probably will.

So in this example we can be 95% confident that the interval between 120mmHg and 150mmHg represents a plausible range of values for the true mean systolic blood pressure. And that's as precise as we can be (with this sized sample).

If we wanted to be even more confident, then we could calculate the 99% confidence interval. Suppose this is (105 to 165) mmHg. Notice that this interval is wider (and thus less precise and less useful), than the 95% confidence interval. The more confident we want to be, the wider the confidence interval has to become. It is also worth noting that larger sample sizes produce narrower (more precise) intervals, because of course the larger a sample is the more representative it is likely to be.

**Q. 6.1** Researchers investigating the prevalence\* of genital chlamydia in a population of women aged 18 to 50, used a sample of 200 women and calculated a sample mean prevalence of 0.03 with a 95% confidence interval for the true prevalence of (0.010 to 0.050). (a) What is the value of the relevant sample statistic; (b) Explain and interpret the confidence interval.

### Standard error

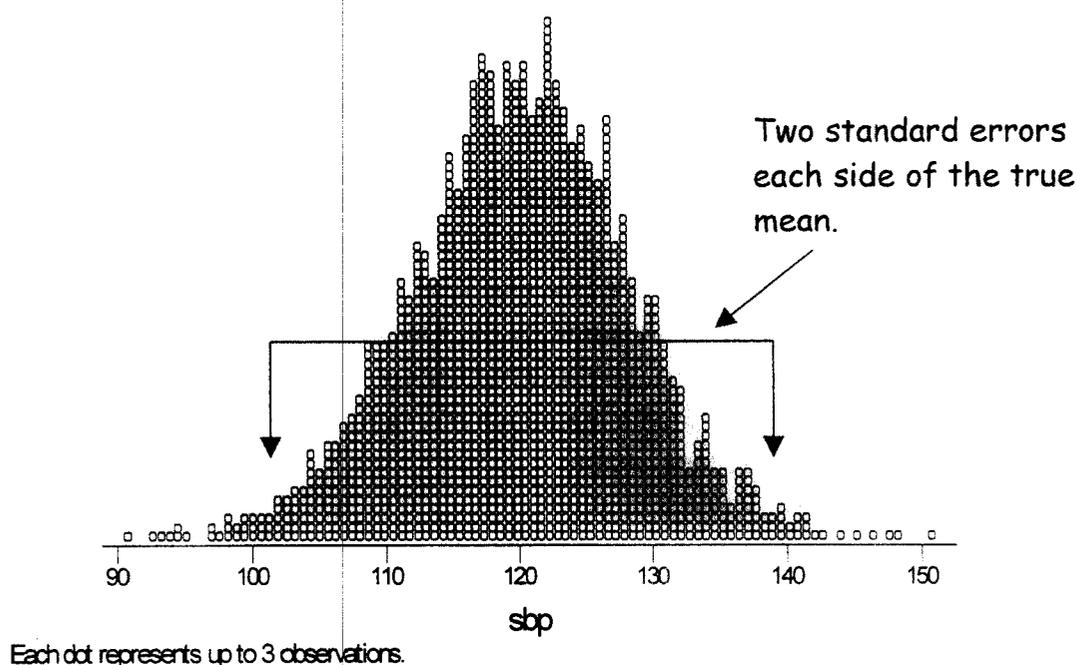
Calculation of confidence intervals for a population parameter is based upon what is known as the **standard error**. Since the concept of standard error is fundamental to the whole idea of statistical inference, we need to devote a little time to an explanation of this important idea. To explain what this is, suppose we could take *all* possible different same-size samples from a population. In theory, for any population of reasonable size, we will be able to take a great

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\* *Prevalence* measures the proportion of individuals in a population who have some condition at some moment in time.

many such samples. For example, with a population of just 60 subjects we could take 75,000,000,000 different samples each of size 10.\* If for each of these different samples we calculate the sample mean we'll end up with a very large number of different sample mean values.

Surprisingly, if we could plot these sample mean values, with a dotplot for example, we would find that they are distributed *Normally*! What's more the distribution is *centred around the true population mean*. These ideas are illustrated in the dotplot in Figure 6.1 where each dot represents the sample mean systolic blood pressure for each of all possible samples taken from a population. The sample means locate around the true population mean of 120mmHg.



**Figure 6.1** Dotplot showing distribution of all possible sample mean systolic blood pressures from a population. The distribution is Normal and centred around the true population mean and its spread is measured by what is known as the *standard error*.

Now like *any* Normal distribution, the distribution of sample means has the same area properties described in Unit 4. In particular, two standard errors either side of the mean (the true population mean) will include about 95% of the sample means. Put another way, about 95% of sample means will never be further away than two standard errors from the true mean.

\* The mathematically minded will recall that the number of different samples each of size  $x$  that can be taken from a population of size  $N$  is equal to  $N!/(N-x)!x!$

Bear in mind that all this is theoretical. In practice we usually get to take only *one* sample, and calculate only *one* sample mean. We know only two things: that our single sample mean will lie somewhere in a Normal distribution like that shown above; and that this distribution will be centred around the true population mean (and moreover is probably no further than two  $s.e.(\bar{x})$ s from the true mean). Obviously, the smaller the spread in the sample mean distribution (i.e. the smaller the standard error,  $s.e.(\bar{x})$ ), the closer on average to the true mean any single sample mean necessarily has to be.

In other words, the smaller the standard error, the more precise any single sample mean is likely to be.

**Q. 6.2** A researcher investigating mean systolic blood pressure in an elderly hospitalised population takes a sample of 100 subjects and finds that the sample mean systolic blood pressure is 120mmHg with a  $s.e.(\bar{x})$  of 0.80mmHg. The researcher can be 95% confident that her sample mean lies no further than how far from the true population mean systolic blood pressure?

**Q. 6.3** Are the statements (a) to (d) true or false. A 95% confidence interval for a population mean :

- (a) is wider than a 99% confidence interval;
- (b) includes 95% of the values in a population;
- (c) defines a range of plausible values for the population mean;
- (d) is centred on the sample mean.

**Q. 6.4** The data in Figure 6.2 is taken from a case-control study into integrated asthma care. (a) Interpret the 95% confidence intervals for true mean age in: (i) the education group; and (ii) the control group. (b) These confidence intervals overlap. What do you think this implies about the two population means?

TABLE 1—Patient characteristics at entry into Grampian asthma study of integrated care. Values are means (95% confidence intervals) unless stated otherwise

Characteristics	Education group (n = 352)	Control group (n = 354)
Age	50.1 (48.5 to 51.8)	49.4 (47.8 to 51.0)
Forced expiratory volume in one second (% of predicted)	75.0 (72.2 to 77.8)	77.9 (75.1 to 80.7)
Peak expiratory flow rate	339.1 (327 to 351)	350.7 (338 to 363)
Duration of asthma (years)*	9.8 (8.7 to 11.1)	10.1 (9.0 to 11.4)
No of hospital admissions in previous year*	0.22 (0.17 to 0.25)	0.22 (0.17 to 0.25)
No (%) of men	175 (44)	172 (43)
No (%) of patients with peak flow meter	254 (64)	263 (65)

\*Geometric means.

Figure 6.2 Baseline characteristics of subjects in case-control asthma care study. *BMJ*, 1994, 308.

Confidence intervals can be calculated for a single population mean or proportion (metric data) or for a single median (ordinal data), but the most common applications are those involving *differences* between *two* population parameters, and it is on these that we will now focus.

### Confidence intervals for differences in means

In the above example we discussed confidence intervals in the context of a single population parameter (the population mean). However, confidence intervals are used in clinical research primarily to determine whether there is a statistically significant difference between *two* population parameters. For example between the population mean systolic blood pressure of males and of females. If the *difference* between the two means is *not* zero, then the means *cannot* be the same.

So we calculate a confidence interval to estimate the true difference between the two population means and see if it includes zero (or not). The rule is:

if the 95% (or 99%) confidence interval for the difference between two population means contains the value 0, then the difference between the two means is judged not statistically significant (i.e. the two population means are probably the same).

The confidence interval will contain 0 only when the lower limit of the interval is negative and the upper limit positive. For example, suppose the 95% confidence

interval for the difference between male and female mean systolic blood pressures was (-3 to 6) mmHg. Since this interval contains 0, we would conclude, with 95% confidence, that there was no statistically significant difference between the true means (we try not to worry about the 5% chance that we may be wrong).

In the study reported in Figure 6.3 the authors were investigating differences in mean bone mineral densities (bmd) between depressed and "normal" women.

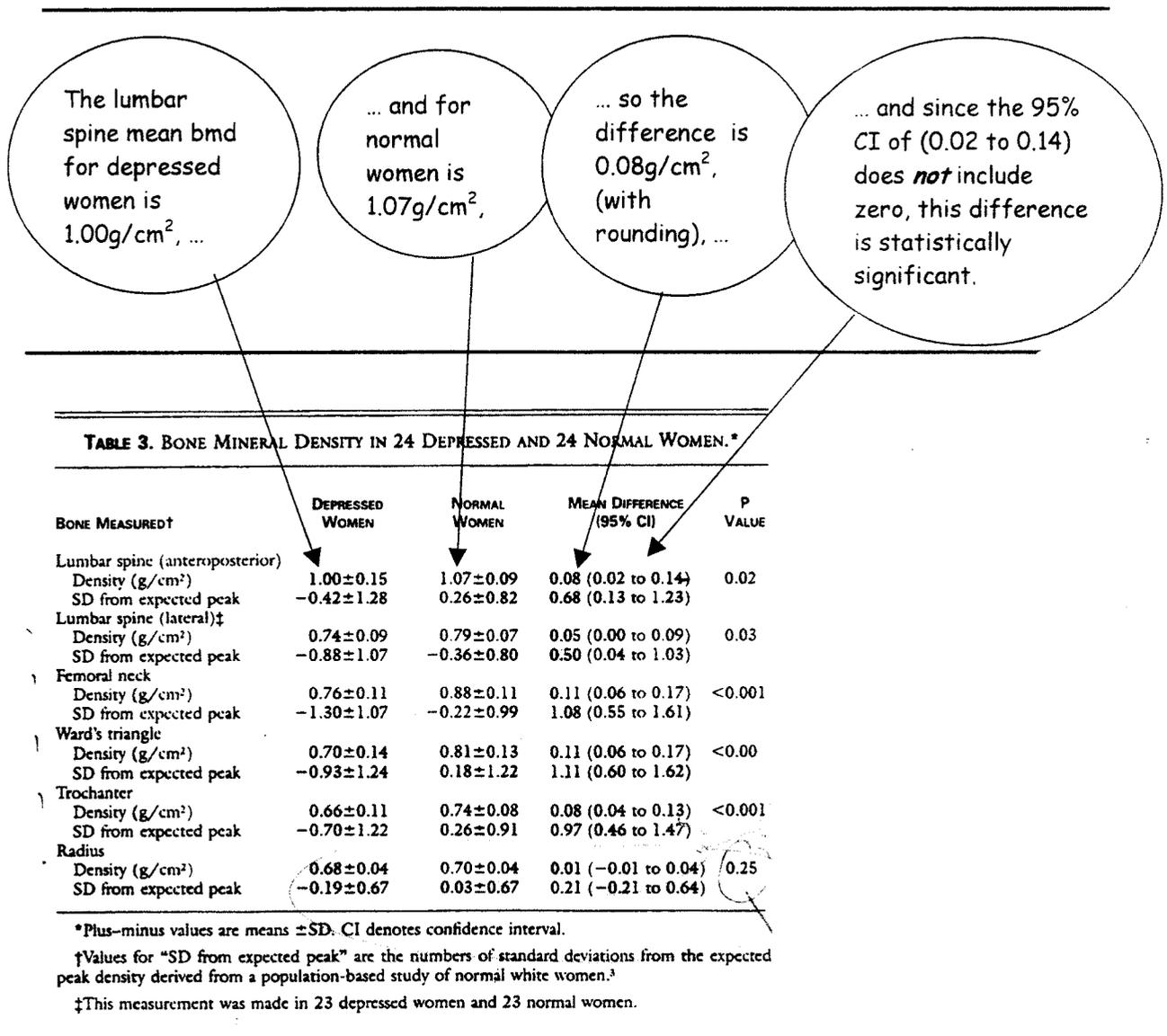


Figure 6.3 Bone mineral density in depressed and normal women. NEJM, 1996.

In the second and third columns of the table they provide sample estimates of the true mean bone densities at six sites, for both depressed and normal of

women (the  $\pm$  values are the s.d.s). The fourth column contains estimates of the *differences* in mean bone densities along with the 95% confidence intervals for these differences (ignore the "SD from expected peak" rows).

Thus at the lumbar spine the mean bone mineral density for the sample of depressed women was  $1.00\text{g/cm}^2$  ( $\text{SD} = 0.15\text{g/cm}^2$ ), for the non-depressed women it was  $1.07\text{g/cm}^2$  ( $\text{SD} = 0.09\text{g/cm}^2$ ). The difference in sample means is thus  $0.08\text{g/cm}^2$  ( $1.07$  minus  $1.00$ , allowing for rounding errors). So the mean bone density at the lumbar spine is somewhere around  $0.08\text{g/cm}^2$  more dense in the normal women than in the depressed women. The 95% confidence interval for the difference in means will provide a plausible range for the true difference. This is (0.02 to 0.14), which does not contain 0, and we can be 95% confident that there *is* a statistically significant difference in mean bone mineral density at the lumbar spine between the two groups of women. Moreover, a plausible range of values for the true difference is between  $0.02$  and  $0.14\text{g/cm}^2$ .

**Q. 6.5** Interpret the 95% confidence intervals for the other five sites in Figure 6.3.

### Confidence intervals for the difference in two proportions or percentages

The same rule applies in this situation as with the difference between two means. If the confidence interval contains 0, then the two population proportions are not significantly different.

As an example, consider the following case-control study with which the authors investigated the effects of improving nutrition on respiratory infections and diarrhoeal disease in Vietnamese pre-school children (Figure 6.4). They compared the incidence and severity of these two illnesses in the children two communes, one which had benefited from an Australian nutrition project from 1991 to the end of 1993 (the cases), the other which had received no such input (the controls).

The children were surveyed every three months from March 1992 until April 1993, i.e. there were five data collection periods. In Figure 6.4 the authors provide 95% confidence intervals for the difference in the percentage of children in the two communes who suffered diarrhoeal disease (dd) in the two-week period prior to each data collection period.

The results indicate that at the beginning of the study (Collection periods 1 and 2) the proportion of children with levels of diarrhoeal disease were much higher

in the treatment commune (Khai Xuan), but as the benefits of the nutrition project took effect (Collection periods<sup>3,4</sup> and 5), levels fell until they were no longer statistically significantly different from the lower levels in the control commune (Ching Cong)

Q. 6.6 Interpret the 95% confidence intervals for the difference in the percentage of children in the two communes with diarrhoeal disease in Periods 2 to 5.

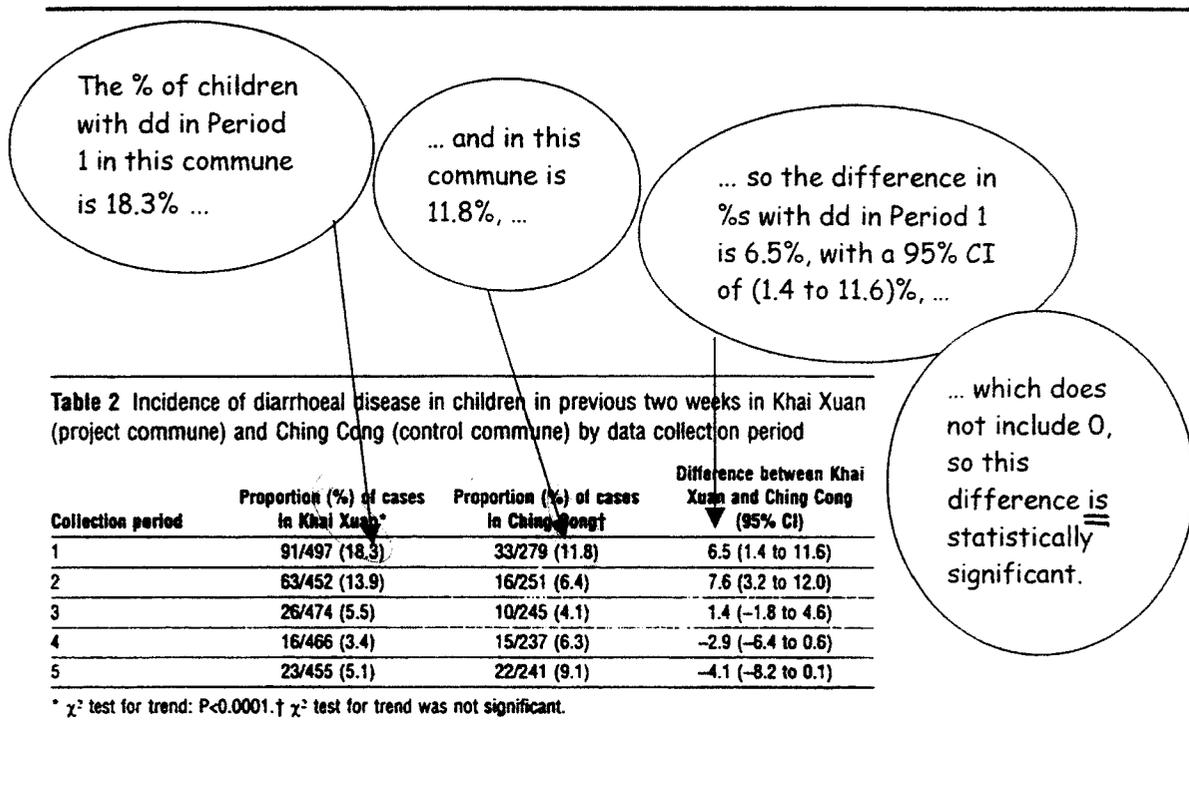


Figure 6.4 Proportion of children in two Vietnamese communes with diarrhoeal disease. *BMJ*, 1997, 315.

### Confidence intervals for the difference between two medians

If the data is metric (but skewed) or ordinal we might choose to compare two *medians* as the most appropriate measures of location. But the rule for interpreting the confidence interval is the same as above. If the confidence interval for the difference between two medians includes 0 then the two population medians are not significantly different.

As an example, we can return to the post-operative stump pain study first encountered in Q. 4.6. Patient pre-amputation pain was measured in both the treatment and control groups. Figure 6.5 shows the median pain levels for the two groups, the difference in the two medians, and the 95% confidence intervals for the difference.

The results shows that after the epidural bolus (of either bupivacaine or saline) the median pain levels of the treatment and control groups were 0 and 38 respectively. Thus the difference was 38 and the 95% confidence interval for the true difference was (24 to 43). This interval does not include 0, so the difference between the two groups is statistically significant. Put another way, a plausible range for the true difference in median pain levels is that it is somewhere between 24 and 43.

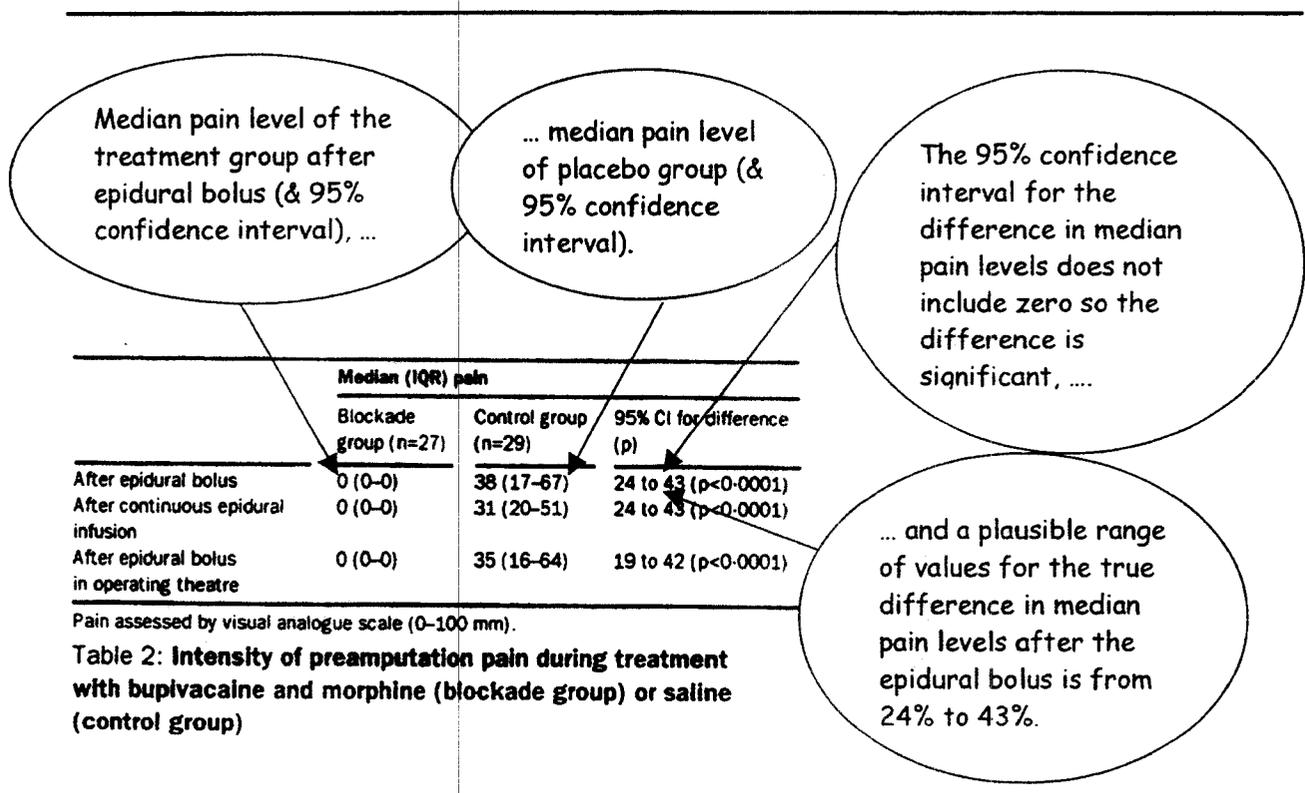


Figure 6.5 Median pre-operative pain levels in stump pain study. The Lancet, 1997, 350.

Q. 6.7 (a) Interpret the 95% confidence interval for the median level of pain of the control group after the epidural bolus. (b) Interpret the 95% confidence

intervals for the difference in median pain levels between the two groups: (i) after continuous epidural infusion; and (ii) after epidural bolus in the operating theatre.

Confidence intervals are used in many contexts. The general rule for all of them when the difference between two population parameters is expressed in terms of a confidence interval is:

if the interval *contains* 0, then we can say with a confidence (usually) of 95% that there is *no* statistically significant difference between the two parameter values. When the confidence interval does *not* contain 0, then there *is* a statistically significant difference.

### Confidence intervals for the ratio of two means or proportions

The above rule does not apply when, instead of the *difference* between means, proportions, medians, and so on, the results are expressed in terms of the ratio of two of these parameters. In these situations we look, not to see if the confidence interval contains 0, indicating no significant difference, but whether the interval contains 1. Clearly, if the ratio of two means, say, is equal to 1, then the means must be the same. When the estimated ratio departs from 1, we need a confidence interval to judge whether this is likely to be due to chance alone or whether it marks a significant difference.

As an example, the authors of the study first referred to in Figure 6.2 used this approach to measure the efficacy of a computer-supported education programme in reducing hospital admissions for asthma patients. One group received the enhanced education programme (four booklets sent by post), the other (control) group received conventional oral education during clinic or outpatient visits. Figure 6.6 contains the means (along with the 95% CIs) for a number of clinical outcomes for two groups of patients and the ratios of these means (with their 95% confidence intervals). The ratios - the mean of the education group divided by the mean of the conventional group - are calculated to enable the outcomes in the two groups to be compared. If this ratio is greater than 1, then use in the education group is greater, if less than one, smaller, and if equal to 1, the same. The authors of the study were hoping to demonstrate that the education group would make less use of services.

Q. 6.8 (a) Interpret the 95% confidence interval for the mean number of bronchodilators prescribed in the *control* group. (b) For which clinical outcome(s) is there a statistically significant difference in the means of the two groups. Explain.

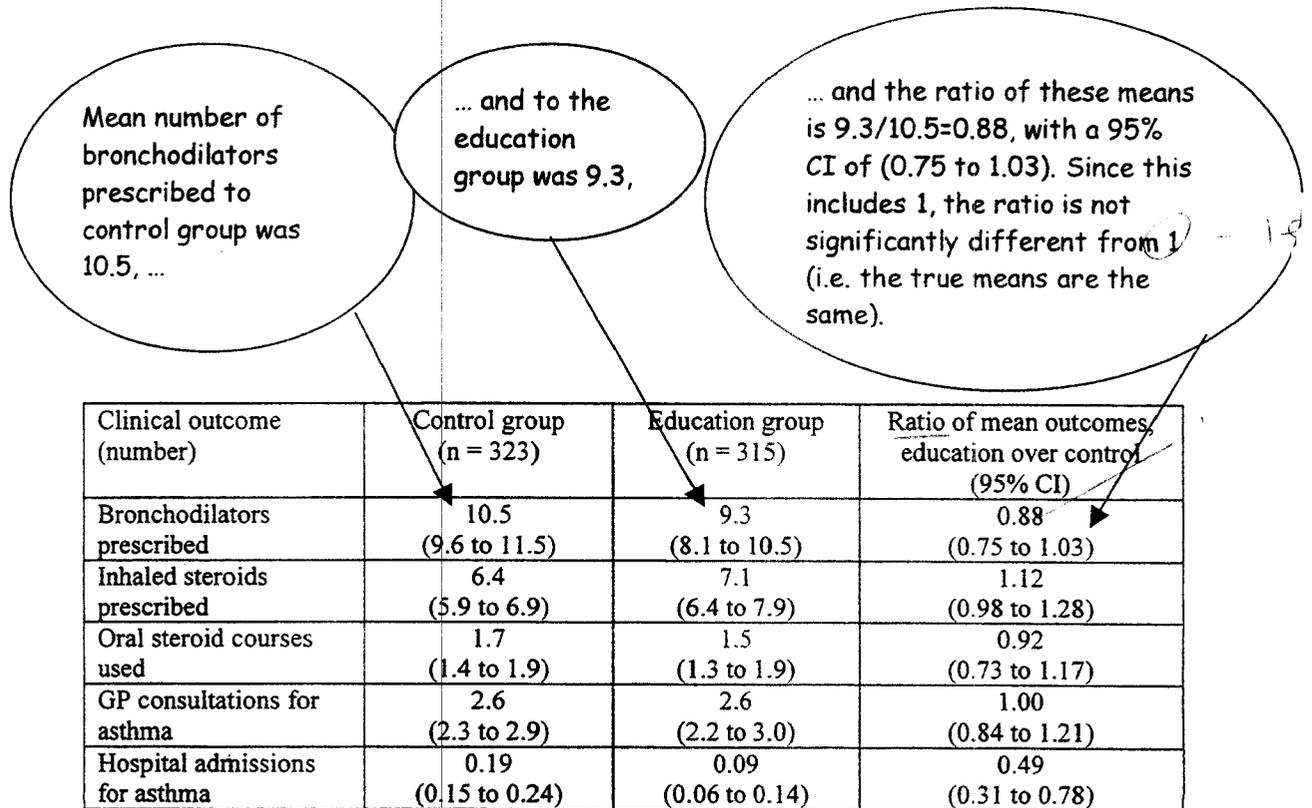


Figure 6.6 Reducing hospital admission through computer supported education for asthma patients. *BMJ*, 308.

### Confidence intervals for risk and odds ratios

We discussed risk and odds ratios in Unit 5 and as an example calculated the risk ratio for coronary heart disease (CHD) for smokers compared to non-smokers to be 12.31. But this result might have occurred by chance. The sample risk ratio is after all only an *estimate* of the true (population) risk ratio which itself might not be different from 1. We need to examine the confidence interval before we can decide whether this is a statistically significant result (i.e. is also true in the population).

The rule is the same as for the ratios of two means discussed above. If the confidence interval for the risk or odds ratio includes 1, then we can interpret this as meaning that this result could have arisen by chance alone, and in the population the odds ratio is probably not significantly different from 1 (i.e. smoking is not a significant risk factor for CHD).

**If the 95% confidence interval for the risk or odds ratio includes 1 then there is probably no significant difference between the two risks or the two odds.**

As an example, consider Figure 6.7 taken from a study into risk factors for genital chlamydia (you first encountered this study in Q.5.9). One potential risk factor was age. The results show that for women aged  $\leq 20$ , the odds for of genital chlamydia were over eight times those for women  $\geq 31$  (this latter group is taken as the referent group). The 95% confidence interval of (2.28 to 32.80) does not include 1, so being aged  $\leq 21$  is a statistically significant risk for this disease.

**Q. 6.9** Interpret the odds and their 95% confidence intervals in Figure 6.7 for: (a) marital status; (b) number of (sexual) partners in the past year; (c) one or more *new* (sexual) partners in the past three months. Note: we first encountered this study in Q. 5.9.

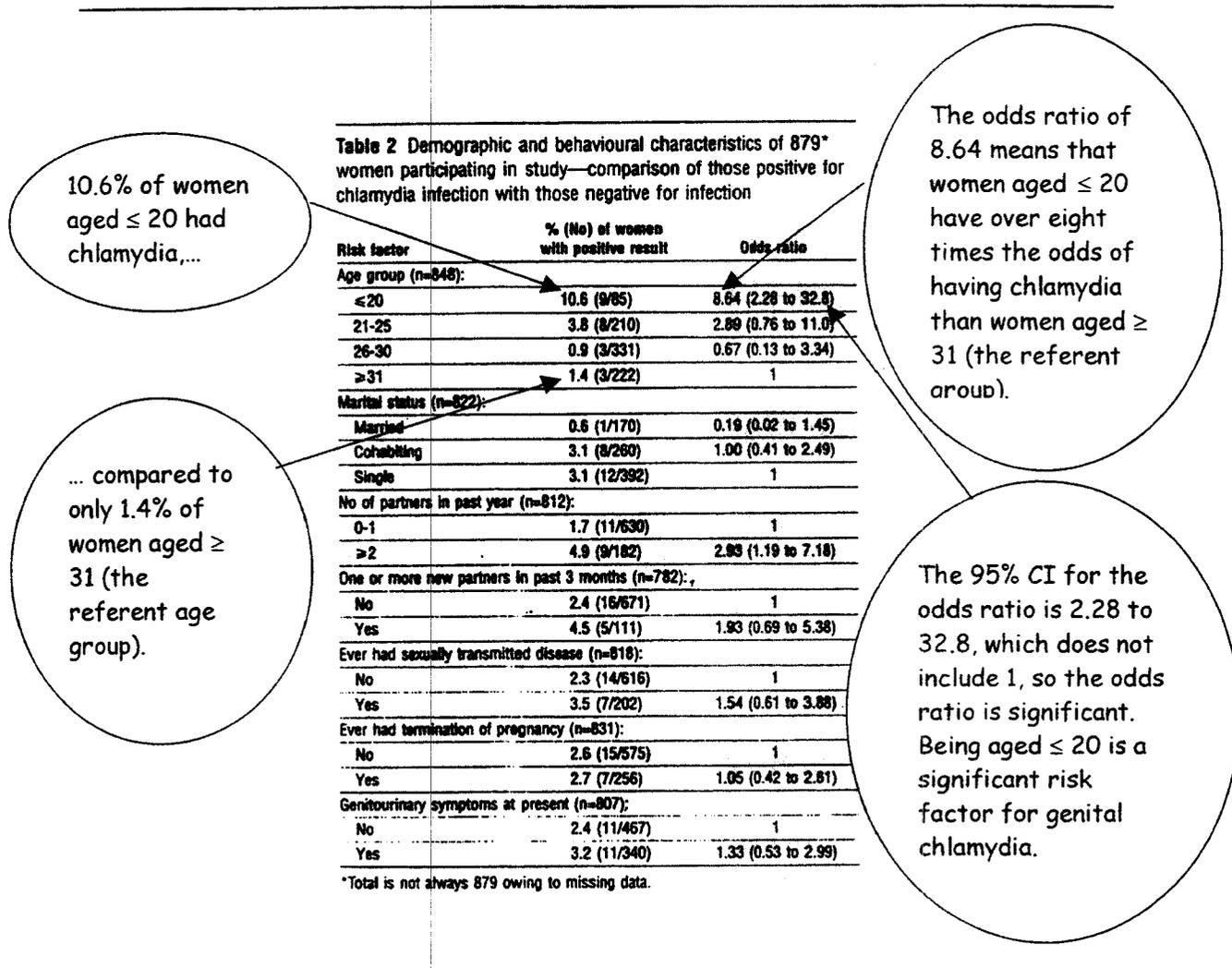


Figure 6.7 Risk factors for genital chlamydia, their odds ratios and 95% confidence intervals. *BMJ*, 315, 1997.

## Unit 6 Confidence intervals

## Solutions to questions

Q. 6.1 (a) The sample statistic is the sample mean prevalence of 0.03; (b) We can be 95% confident that the true population prevalence is somewhere in the interval from 0.010 to 0.05 (or from 1% to 5%).

Q. 6.2 No further than  $2 \times 0.8\text{mmHg}$  or  $1.6\text{mmHg}$  from the true population mean systolic blood pressure in either direction.

Q. 6.3 (a) False - the higher the confidence level, the wider the confidence interval; (b) False - it includes 95% of all possible sample means; (c) True - this is one way to define a confidence interval; (d) True - because the confidence interval is equal to the sample mean  $\pm$  the same amount.

Q. 6.4 (a) (i) The interval from 48.5 years to 51.8 years represents a plausible range of values for the true (population) mean age of those in the educated group. Or, there is a 95% chance that the interval from 48.5 years to 51.8 years contains the true (population) mean age for this group. (ii) A similar interpretation except that the interval for the control group is 47.8 years to 51.0 years.

(b) That the true (population) mean ages could well be the same.

Q. 6.5 The other confidence intervals in Figure 6.3 show that all differences in mean bone density are significant (normal women have denser bones than depressed women), since none of the confidence intervals contain 0, *except* for the radius. Here the interval is from  $-0.01\text{g/cm}^2$  to  $0.04\text{g/cm}^2$ , which does include zero. Since zero is a possible value it can't be ruled out as being the true value.

Q. 6.6 In period 2 there is a statistically significant difference in the two population percentages with diarrhoeal disease since the 95% confidence interval (from 3.2 to 12.0) does not include 0. For collection times 3 to 5 the differences in the two percentages are not statistically significant since all of the confidence intervals include 0.

Q. 6.7 (a) The level of pain in the control group is 38 with a 95% confidence interval of (17 to 67). This means that a plausible range for the true pain level in this group is from 17 to 67. (b) There is a significant difference in median pain levels between the two groups at both stages, because neither of the CIs includes 0.

Q. 6.8 (a) In the control group the mean number of bronchodilators prescribed was 10.5 with a 95% confidence interval of (9.6 to 11.5). So this interval represents a plausible range of values for the true mean number prescribed.

(b) The table shows that for all of the outcomes, except the mean number of hospital admissions, the 95% confidence interval for the ratio of the population means contains 1, thus there is no difference in the means of these outcomes between the groups for the first four outcomes. For the ratio of the mean number of hospital admissions, the educated group had only 49% the number of admissions as the control group, with a 95% confidence interval of (0.31 to 0.78). Since this does not contain 1, the difference between the groups for this outcome is significant. A plausible range of values for the true ratio for this outcome is from 0.31 (31%) to 0.78 (78%).

Q. 6.9 (a) The referent group here is defined as single women (since this is the one where the odds ratio = 1). Compared to these, married women in the sample had an odds ratio of 0.19. At first sight this suggests that being married is therefore a protective factor against genital chlamydia, married women have only about a fifth ( $1/0.19$ ) the odds of contracting the disease compared to single women. However in this case the 95% confidence interval, given as (0.02 to 1.45) includes the value 1, so we can conclude that being married (compared to being single) is not a statistically significant risk factor for genital chlamydia.

(b) Odds ratio for chlamydia among women with  $\geq 2$  partners, compared to women with 0 or 1 partners (the referent group) is 2.93. The confidence interval (1.19 to 7.18) does not include 0, so multiple partners is a statistically significant risk factor for chlamydia. (c) Odds ratio for chlamydia is 1.93 for subjects with one or more new (sexual) partners in the past three months, compared to those with none. But confidence interval (0.69 to 5.38) includes 1 so this variable is not a statistically significant risk factor.