



home / math / confidence interval calculator Use this calculator to compute the confidence interval or margin of error, assuming the sample mean most likely follows a normal distribution. Use the Standard Deviation Calculator if you have raw data only. What is the confidence interval? In statistics, a confidence interval is a range of values that is determined through the use of observed data, calculated at a desired confidence level that may contain the true value of the parameter being studied. The confidence level, relates to how reliable the estimation procedure is, not the degree of certainty that the computed confidence interval contains the true value of the parameter being studied. The desired confidence level is chosen prior to the computation of the confidence intervals, that when constructed given the chosen confidence intervals are typically written as (some value) ± (a range). The range can be written as an actual value or a percentage. It can also be written as simply the range of values. For example, the following are all equivalent confidence intervals: 20.6 ±0.887 or 20.6 ±4.3% or [19.713 - 21.487] Calculating confidence intervals: Calculating a confidence interval involves determining the sample mean, X, and the population standard deviation, s, can be used, then the sample size is greater than 30. For a sample size greater than 30, the population standard deviation and the sample standard deviation will be similar. Depending on which standard deviation is known, the equation used to calculate the confidence interval differs. For the purposes of this calculator, it is assumed that the population standard deviation is similar. Only the equation for a known standard deviation is shown. Where Z is the Z-value for the chosen confidence level, \bar{X} is the sample mean, σ is the standard deviation, and n is the sample size. Assuming the following with a confidence level of 95%: $X = 22.8 \ Z = 1.960 \ \sigma = 2.7 \ n = 100$ The confidence interval is: 22.8 ±0.5292 Z-values for Confidence Intervals Confidence Intervals Confidence level of 95%: $X = 22.8 \ Z = 1.960 \ \sigma = 2.7 \ n = 100$ The confidence interval is: 22.8 ±0.5292 Z-values for Confidence Intervals Confidence Inte Intervals Author: Lisa Sullivan, PhD Professor of Biostatistics Boston University School of Public Health Introduction As noted in earlier modules a key goal in applied biostatistics is to make inferences about unknown population parameters based on sample statistics. There are two broad areas of statistical inference, estimation and hypothesis testing. Estimation is the process of determining a likely value for a population parameter (e.g., the true population mean or population parameter. The sample should be representative of the population, with participants selected at random from the population. In generating estimates, it is also important to quantify the precision of estimates from different samples. Learning Objectives After completing this module, the student will be able to: Define point estimate, standard error, confidence level and margin of error Compare and contrast standard error and margin of error Compute and interpret confidence intervals for means and proportions Differentiate independent and matched or paired samples Compute confidence intervals for the difference in means and proportions in independent samples and for the mean difference in paired samples Identify the appropriate confidence interval formula based on type of outcome variable and number of samples of potential interest when one is estimating health outcomes (or "endpoints"). Many of the outcomes we are interested in estimating are either continuous or dichotomous variables, although there are other types which are discussed in a later module. The parameters to be estimated depend not only on whether the endpoint is continuous or dichotomous, but also on the number of groups being studied. Moreover, when two groups are being compared, it is important to establish whether the groups are independent (e.g., men versus women) or dependent (i.e., matched or paired, such as a before and after comparison). The table below summarizes parameters Being Estimated Continuous Variable One Sample mean proportion or rate, e.g., prevalence, cumulative incidence, incidence rate Two Independent Samples difference in means difference in proportions or rates, e.g., risk difference, rate difference, rate difference, rate difference, rate difference in means difference in proportions or rates, e.g., risk difference, rate difference in means difference, rate difference, rate difference, rate difference, rate difference, rate difference, rate difference in means difference in proportions or rates, e.g., risk difference, rate difference, r interval (CI) estimate. For both continuous variables (e.g., population mean) and dichotomous variables (e.g., population proportion) one first computes the point estimate from a sample means and sample means and sample proportions are unbiased estimates of the corresponding population parameters. For both continuous and dichotomous variables, the confidence interval estimate (CI) is a range of likely values for the population parameter based on: the point estimate, e.g., the sample mean the investigator's desired level of confidence (most commonly 95%, but any level between 0-100% can be selected) and the sampling variability or the stimate. Strictly values for the point estimate. speaking a 95% confidence interval means that if we were to take 100 different samples and compute a 95% confidence intervals will contain the true mean value (µ). In practice, however, we select one random sample and generate one confidence interval, which may or may not contain the true mean. The observed interval may over- or underestimate μ . Consequently, the 95% CI is the likely range of the true, unknown parameter. The confidence interval does not reflect the variability in the unknown parameter. Rather, it reflects the amount of random error in the sample and provides a range of values that are likely to include the unknown parameter. Another way of thinking about a confidence interval is that it is the range of likely values of the parameter (defined as the point estimate + margin of error) with a specified level of confidence interval is that it is the range of likely values of the parameter (defined as the point estimate + margin of error) with a specified level of confidence interval is that it is the range of likely values of the parameter (defined as the point estimate + margin of error) with a specified level of confidence interval is that it is the range of likely values of the parameter (defined as the point estimate + margin of error) with a specified level of confidence interval is that it is the range of likely values of the parameter (defined as the point estimate + margin of error) with a specified level of confidence (which is similar to a probability). mean. This means that there is a 95% probability that the confidence interval will contain the true population mean. Thus, P([sample mean] - margin of error) = 0.95. The Central Limit Theorem introduced in the module on Probability stated that, for large samples, the distribution of the sample means is approximately normally distributed with a mean: and a standard deviation (also called the standard error): For the standard normal distribution, P(-1.96 < Z < 1.96) = 0.95, i.e., there is a 95% probability that a standard normal variable, Z, will fall between -1.96 and 1.96. The Central Limit Theorem states that for large samples: By substituting the expression on the right side of the equation: Using algebra, we can rework this inequality such that the mean (µ) is the middle term, as shown below. then and finally This last expression, then, provides the 95% confidence interval for the population mean, and this can also be expressed as: Thus, the margin of error is 1.96 times the standard error (the standard deviation of the point estimate from the sample), and 1.96 reflects the fact that a 95% confidence level (e.g., for a 95% confidence level, was selected. So, the general form of a confidence level (e.g., for a 95% confidence level, e.g., for a 95% confidence level, e.g., for a 95% confidence level (e.g., for a 95% confidence level, e.g., for a 95% confidence level (e.g., for a 95% confidence level, e.g., for a 95% confidence level (e.g., for a 95% confidence level, e.g., for a 95% confidence level (e.g., for a 95% confidence level, e.g., for a 95\% confidence level Z=1.96). In practice, we often do not know the value of the population standard deviation (σ). However, if the sample size is large (n > 30), then the sample size is large (n > 30), then the sample standard deviation. Table - Z-Scores for Commonly Used Confidence Intervals Desired Confidence Interval Z Score 90% 95% 99% 1.645 1.96 2.576 In the health-related publications a 95% confidence interval is most often used, but this is an arbitrary value, and other confidence interval, because it allows one to be more confident that the unknown population parameter is contained within the interval. Confidence Interval Estimates for Smaller Samples (n< 30) the Central Limit Theorem does not apply, and another distribution must be used. The t distribution is similar to the standard normal distribution but takes a slightly different shape depending on the sample size. In a sense, one could think of the t distribution as a family of distributions for smaller samples. Instead of "Z" values, there are "t" values for confidence intervals which are larger for smaller samples. Instead of "Z" values, there are "t" values for confidence intervals which are larger for smaller samples. large samples, the t distribution assumes that the outcome of interest is approximately normally distributed. A table of t values is shown in the frame below. Note that the table can also be accessed from the "Other Resources" on the right side of the page. mean systolic blood pressure, body mass index, total cholesterol level or white blood cell count in a single target population. We select a sample size (n), the sample mean, and the sample mean, and the sample standard deviation (s). The formulas for confidence intervals for the population mean depend on the sample size and are given below. Confidence Intervals for μ Use the Z table for the standard normal distribution. Use the t table with df=n-1 Example: Descriptive statistics on variables measured in a sample of a n=3,539 participants attending the 7th examination of the offspring in the Framingham Heart Study are shown below. Characteristic n Sample Mean Standard Deviation (s) Systolic Blood Pressure 3,534 127.3 19.0 Diastolic Blood Pressure 3,532 74.0 9.9 Total Serum Cholesterol 3,310 200.3 36.8 Weight 3,326 65.957 3.749 Body Mass Index 3,326 65.957 3.749 Body Mass Index 3,326 28.15 5.32 following formula: The Z value for 95% confidence is Z=1.96. [Note: Both the table of Z-scores and the table of t-scores can also be accessed from the "Other Resources" on the right side of the page.] Substituting the sample statistics and the Z value for 95% confidence, we have So the confidence interval is (126.7,127.9) A point estimate for the true mean systolic blood pressure in the population is 127.3, and we are 95% confident that the true mean is between 126.7 and 127.9. The margin of error is very small here because of the large sample size What is the 90% confidence interval for BMI? (Note that Z=1.645 to reflect the 90% confidence level.) Answer The table below shows data on a subsample of n=10 participants in the 7th examination of the Framingham Offspring Study. Characteristic n Sample Mean Standard Deviation (s) Systolic Blood Pressure 10 71.3 7.2 Total Serum Cholesterol 10 202.3 37.7 Weight 10 176.0 33.0 Height 10 67.175 4.205 Body Mass Index 10 27.26 3.10 Suppose we compute a 95% confidence interval for the true systolic blood pressure using data in the subsample. Because the sample size is small, we must now use the confidence interval formula that involves t rather than Z. The sample size is n=10, the degrees of freedom (df) = n-1 = 9. The t value for 95% confidence with df = 9 is t = 2.262. Substituting the sample statistics and the t value for 95% confidence, we have the following expression: . Interpretation: Based on this sample, we are 95% confident that the true systolic blood pressure in the population is 121.2. Based on this sample, we are 95% confident that the true mean systolic blood pressure in the population is between 113.3 and 129.1. Note that the margin of error is larger here primarily due to the small sample size. Using the subsample in the table above, what is the 90% confidence Interval for BMI? Answer Confidence Interval for One Sample, Dichotomous Outcome Suppose we wish to estimate the proportion of people with diabetes in a population or the proportion of people with hypertension or obesity. These diagnoses are defined by specific levels of laboratory tests and measurements of blood pressure and body mass index, respectively. Subjects are defined as having these diagnoses or not, based on the definitions. When the outcome of interest is dichotomous like this, the record for each member of the sample indicates having the condition or characteristic of interest or not. Recall that for dichotomous outcomes the investigator defines one of the outcomes a "successe" in the sample. For example, if we wish to estimate the proportion of people with diabetes in a population, we consider a diagnosis of diabetes as a "success" (i.e., and individual who has the outcome of interest), and it is computed by taking the ratio of the number of successes in the sample to the sample size, that is: $\hat{p} = x/n$ Confidence Interval for the Population Proportion If there are more than 5 failures, then the confidence interval can be computed with this formula: The point estimate for the population proportion is the sample proportion, and the margin of error is the product of the Z value for the desired confidence level (e.g., Z=1.96 for 95% confidence) and the standard error of the point estimate is: This formula is appropriate for large samples, defined as at least 5 successes and at least 5 failures in the sample. This was a condition for the Central Limit Theorem for binomial outcomes. If there are fewer than 5 successes or failures then alternative procedures, called exact methods, must be used to estimate the population proportion.1,2 Example: During the 7th examination of the Offspring cohort in the Framingham Heart Study there were 1219 participants being treated for hypertension and 2,313 who were not on treatment. If we call treatment a "success", then x=1219 and n=3532. The sample proportion of the proportion is: This is the point estimate of the proportion of the proportion is 34.5%. The sample is large, so the confidence interval can be computed using the formula: Substituting our values we get which is So, the 95% confidence interval is (0.329, 0.361). Thus we are 95% confident that the true proportion of persons on antihypertensive medication is between 32.9% and 36.1%. Specific applications of estimation for a single population with a dichotomous outcome involve estimating prevalence. cumulative incidence, and incidence rates. The table below, from the 5th examination of the Framingham Offspring cohort, shows the number of men and women found with or without cardiovascular disease (CVD). Estimate the prevalence of CVD in men using a 95% confidence interval. Free of CVD Total Men 1,548 244 1,792 Women 1,872 135 2,007 Total 3,420 379 3,799 Answer Confidence Interval for Two Independent Samples, Continuous Outcome There are many situations where it is of interest to compare two groups with respect to their mean and women, or perhaps compare body mass index (BMI) in smokers and non-smokers. Both of these situations involve comparisons between two independent groups, meaning that there are different people in the groups being compared. We could begin by computing the sample sizes (n1 and n2), means (and), and standard deviations (s1 and s2) in each sample. In the two independent samples application with a continuous outcome, the parameter of interest is the difference in population means is the difference in sample means. The confidence interval will be computed using either the Z or t distribution for the selected confidence level and the standard error of the point estimate. The use of Z or t again depends on whether the sample sizes are large (n1 > 30 and n2 > 30) or small. The standard error of the point estimate will incorporate the variability in the outcome of interest in each of the comparison groups. If we assume equal variances between groups, we can pool the information on variability (sample variances) to generate an estimate of the population variability. Therefore, the standard deviation (Sp) (assuming that the variances in the populations are similar) computed as the weighted average of the standard deviations in the samples, i.e.: and the pooled estimate of the common standard deviation is Computing the Confidence Interval for a Difference Between Two Means If the sample sizes are larger, that is both n1 and n2 are greater than 30, then one uses the z-table. If either sample size is less than 30, then the t-table is used. If n1 > 30 and n2 > 30, we can use the z-table: Use Z table for standard normal distribution If n1 < 30 or n2 < 30, use the t-table with degrees of freedom = n1+n2-2 For both large and small samples Sp is the pooled estimate of the common standard deviation (assuming that the variances in the populations are similar) computed as the weighted average of the standard deviations in the samples. These formulas assume equal variability in the two populations, and if the sample variances are similar of the comparison populations, and if the sample variances are similar of the comparison populations. For analysis, we have samples from each of the comparison populations, and if the sample variances are similar of the comparison populations. then the assumption about variability in the populations is reasonable. As a guideline, if the ratio of the sample variances, s12/s22 is between 0.5 and 2 (i.e., if one variance is no more than double the other), then the formulas in the table above are appropriate. If not, then alternative formulas must be used to account for the heterogeneity in variances.3,4 Large Sample Example: The table below summarizes data n=3539 participants attending the 7th examination of the Offspring cohort in the Framingham Heart Study. Men Women Characteristic N s n s Systolic Blood Pressure 1,623 128.2 17.5 1,911 126.5 20.1 Diastolic Blood Pressure 1,622 75.6 9.8 1,910 72.6 9.7 Total Serum Cholesterol 1,544 192.4 35.2 1,766 207.1 36.7 Weight 1,612 194.0 33.8 1,894 157.7 34.6 Height 1,545 68.9 2.7 1,781 63.4 2.5 Body Mass Index 1,545 28.8 4.6 1,781 27.6 5.9 Suppose we want to calculate the difference in mean systolic blood pressures between men and women, and we also want the 95% confidence interval for the difference in mean systolic blood pressures between men and women, and we also want the 95% confidence interval for the difference in mean systolic blood pressures between men and women, and we also want the 95% confidence interval for the difference in mean systolic blood pressures between men and women, and we also want the 95% confidence interval for the difference in mean systolic blood pressures between men and women and wom means. The sample is large (> 30 for both men and women), so we can use the confidence interval formula with Z. Next, we will check the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 and 2, suggesting that the assumption of equality of population variances is 17.52/20.12 = 0.76, which falls between 0.5 a reasonable. First, we need to compute Sp, the pooled estimate of the common standard deviation. Substituting we get which simplifies to Notice that for this example Sp, the pooled estimate of the common standard deviation, is 19, and this falls in between the standard deviation in the comparison groups (i.e., 17.5 and 20.1). Next we substitute the Z score for 95% confidence, Sp=19, the sample means, and the sample sizes into the equation for the confidence interval. Substituting which simplifies to Therefore, the confidence interval is (0.44, 2.96) Interpretation: With 95% confidence interval is (0.44, 2.96) Interpretation: With 95\% confidence interval is (0.44, 2.96) Interpretation: With 95\% confidence interval is (0.44, 2.96) Interpretat best estimate of the difference, the point estimates for a population parameter in a single sample (e.g., the mean [µ]) or population proportion [p]) the resulting confidence interval provides a range of likely values for that parameter. In contrast, when comparing two independent samples in this fashion the confidence interval provides a range of values for the difference in mean systolic blood pressures is between 0.44 and 2.96 units with men having the higher values. In this example, we arbitrarily designated the men as group 1 and women as group 2. Had we designated the groups the other way (i.e., women as group 2), the confidence interval would have been -2.96 to -0.44, suggesting that women have lower systolic blood pressures (anywhere from 0.44 to 2.96 units lower than men). The table below summarizes differences between men and women with respect to the characteristics listed in the first column. The second and third columns show the means and standard deviations for men and women respectively. The fourth columns show the differences between males and the 95% confidence intervals for the differences. (s) Mean (s) 95% CI Systolic Blood Pressure 128.2 (17.5) 126.5 (20.1) (0.44, 2.96) Diastolic Blood Pressure 75.6 (9.8) 72.6 (9.7) (2.38, 3.67) Total Serum Cholesterol 192.4 (35.2) 207.1 (36.7) (-17.16, -12.24) Weight 194.0 (33.8) 157.7 (34.6) (33.98, 38.53) Height 68.9 (2.7) 63.4 (2.5) (5.31, 5.66) Body Mass Index 28.8 (4.6) 27.6 (5.9) (0.76, 1.48) Notice that the 95% confidence interval for the difference in mean total cholesterol levels between men and women is -17.16 to -12.24. Men have lower mean total cholesterol levels than women; anywhere from 12.24 to 17.16 units lower. The men have higher mean values on each of the other characteristics considered (indicated by the positive confidence intervals). The confidence interval for the difference in means provides an estimate of the absolute difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference between comparison groups. It is often of interest to make a judgment as to whether there is a statistically meaningful difference in means provides an estimate of the absolute difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means provides an estimate of the absolute difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means provides an estimate of the absolute difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means of the outcome variable of interest to make a judgment as to whether there is a statistically meaningful difference in means of the outcome variable of interest to make a judgment as to whether the outcome variable of the outcome variable of the ou whether the observed difference is beyond what one would expect by chance. The confidence intervals for the difference in means provide a range of likely values for (µ1-µ2). It is important to note that all values in the confidence intervals for the difference is beyond what one would expect by chance. then the difference will be zero (i.e., (u1-u2) = 0). Zero is the null value of the parameter (in this case the difference in means). If a 95% confidence interval includes the null value, then we conclude that there is a statistically significant difference in means between the groups. For each of the characteristics in the table above there is a statistically significant difference in means are not very different between men and women (e.g., systolic and diastolic blood pressure), yet the 95% confidence intervals do not include zero. This means that there is a small, but statistically meaningful differences are statistically significant if the sample size is sufficiently large, as it is in this example. Small Sample Example: We previously considered a subsample of n=10 participants attending the 7th examination of the Offspring cohort in the Framingham Heart Study. The following table contains descriptive statistics on the same continuous characteristics in the subsample stratified by sex. Men Women Characteristic n Sample Mean s n Sample Mean s Note: Blood Pressure 6 117.5 9.7 4 126.8 12.0 Diastolic Blood Pressure 6 72.5 7.1 4 69.5 8.1 Total Serum Cholesterol 6 193.8 30.2 4 215.0 48.8 Weight 6 196.9 26.9 4 146.0 7.2 Height 6 70.2 1.0 4 62.6 2.3 Body Mass Index 6 28.0 3.6 4 26.2 2.0 Suppose we wish to construct a 95% confidence interval for the difference in mean systolic blood pressures between men and women using these data. We will again arbitrarily designate men group 1 and women group 2. Since the sample sizes are small (i.e., n1< 30 and n2< 30), the confidence interval formula with t is appropriate. However, we will first check whether the assumption of equality of population variances is reasonable. The solution is shown below. First, we compute Sp, the pooled estimate of the common standard deviation: Substituting: Note that again the pooled estimate of the common standard deviation, Sp, falls in between the standard deviations in the comparison groups (i.e., 9.7 and 12.0). The degrees of freedom (df) = n1+n2-2 = 6+4-2 = 8. From the t-Table t=2.306. The 95% confidence interval for the difference in mean systolic blood pressures is: Substituting: Then simplifying further: So, the 95% confidence interval for the difference is 6.84 units and the margin of error is 15.77 units. We are 95% confident that the difference in mean systolic blood pressures between men and women is between -25.07 and 6.47 units. In this sample, the men have lower mean systolic blood pressures than women by 9.3 units. Based on this interval, we also conclude that there is no statistically significant difference in mean systolic blood pressures than women by 9.3 units. confidence interval is a range of likely values for the difference in means. Since the interval contains zero (no difference), we do not have sufficient evidence to conclude that there is a difference), we do not have sufficient evidence to conclude that there is a difference in the difference in the difference). the previous example, because the very small sample size produces a very imprecise estimate of the difference in mean systolic blood pressures. Confidence intervals for the difference in means between two independent groups. There is an alternative study design in which two comparison groups are dependent, matched or paired. Consider the following scenarios: A single sample of participants and each participants and each participant is measured twice, once before and then after an intervention. A single sample of participants and each participants and each participant is measured twice. in a crossover trial). A goal of these studies might be to compare the mean scores measured before and after the intervention, or to compare the mean scores obtained with the two conditions in a crossover study. Yet another scenario is one in which matched samples are used. For example, we might be interested in the difference in an outcome between twins or between siblings. Once again we have two samples, and the goal is to compare the two means. However, the same individual. In the last scenario, measures are taken in pairs of individuals from the same family. When the samples are dependent, we cannot use the techniques in the previous section to compare means. Because the samples are dependency must be used. These techniques that account for the dependency must be used. between twins or sibling pairs). The Unit of Analysis This distinction between independent and dependent samples emphasizes the importance of appropriately identifying the unit of analysis, i.e., the independent entities in a study. In the one sample and two independent samples applications participants are the units of analysis. However, with two dependent samples application, the pair is the unit (and not the number of measurements which is twice the number of units). The parameter of interest is the mean difference, µd. Again, the first step is to compute descriptive statistics. We compute the sample size (which in this case is the number of distinct pairs), the mean and standard deviation of the difference scores, and we denote these summary statistics as n, d and sd, respectively. The appropriate formulas are shown in Table 6.5 and are identical to those we presented for estimating the mean of a single sample, except here we focus on difference scores. Computing the Confidence Intervals for µd Use Z table for standard normal distribution Use t-table with df=n-1 When samples are matched or paired, difference scores are computed for each participant or between members of a matched pair, and "n" is the number of participants or pairs, is the mean of the difference scores, and Sd is the standard deviation of the difference scores Example: In the Framingham Offspring Study, participants attend clinical examinations (i.e., changes over 4 years). The data below are systolic blood pressures measured at the sixth and seventh examinations in a subsample of n=15 randomly selected participants. Since the blood pressure measured at examination 7 from that measured at examination 6 or vice versa. [If we subtract the blood pressure measured at examination 6 from that measured at examination 7, then positive differences represent increases over time.] Subject # Examination 7 Differences represent decreases over time.] Subject # Examination 7 Differences represent decreases over time.] 9 130 131 1 10 137 142 5 11 130 131 1 12 129 135 6 13 112 119 7 14 141 130 -11 15 122 121 -1 Notice that several participants' systolic blood pressure decreased by 27 units from 168 to 141), while others increased (e.g., participant #2's blood pressure increased by 8 units from 111 to 119). We now estimate the mean difference in blood pressures over 4 years. This is similar to a one sample problem with a continuous outcome except that we are now using the difference score = -5.3 and sd = 12.8, respectively. The calculations are shown below Subject # Difference Difference - Mean Difference - Mean Difference - Mean Difference) 1 - 27 - 21.7 470.89 2 8 13.3 176.89 3 - 17 - 11.7 136.89 4 0 5.3 28.09 5 - 30 - 24.7 610.09 6 8 13.3 176.89 7 - 12 - 6.7 44.89 8 - 17 - 11.7 136.89 9 1 6.3 39.69 11 5 - 14.3 18.49 Σ = -79.0 Σ = 0 Σ = 2296.95 Therefore, and We can now use these descriptive statistics to compute a 95% confidence interval for the mean difference in systolic blood pressures in the population. Because the sample size is small (n=15), we use the formula that employs the t-statistic. The degrees of freedom are df=n-1=14. From the table of t-scores (see Other Resource on the right), t = 2.145. We can now substitute the descriptive statistics on the difference is (-12.4, 1.8). Interpretation: We are 95% confidence is (-12.4, 1.8). Interpretation: We are 95% confidence is (-12.4, 1.8). apart) is between -12.4 and 1.8. The null (or no effect) value of the CI for the mean difference in blood pressures over time, because the confidence interval for the mean difference includes zero. Crossover Trials Crossover trials are a special type of randomized trial in which each subject receives both of the two treatments. In many cases there is a "wash-out period" between the two treatments. Outcomes are measured after each treatment in each participant. [An example of a crossover trial with a wash-out period can be seen in a study by Pincus et al. in which the investigators compared responses to analgesics in patients with osteoarthritis of the knee or hip.] A major advantage to the crossover trial is that each participant acts as his or her own control, and, therefore, fewer participants are generally required to demonstrate an effect. When the outcome is continuous, the assessment of a treatment effect in a crossover trial is conducted to evaluate the effectiveness of a new drug designed to reduce symptoms of depression in adults over 65 years of age following a stroke. Symptoms of depression are measured on a scale of 0-100 with higher scores indicative of more frequent and severe symptoms of depression. Patients who suffered a stroke were eligible for the trial. The trial was run as a crossover trial in which each patient received both the new drug and a placebo. Patients were blind to the treatment assignment and the order of treatments (e.g., placebo and then new drug or new drug and then placebo) were measured in each patient. The difference in depressive symptoms was measured in each patient by subtracting the depressive symptom score after taking the placebo from the depressive symptoms After New Drug - Symptoms After Placebo 100 -12.7 8.9 The mean difference in the sample is -12.7 meaning on average patients scored 12.7 points lower on the depressive symptoms scale after taking the new drug as compared to placebo (i.e., improved by 12.7 points on average). What would be the 95% confidence interval for the mean difference in the population? Since the sample size is large, we can use the formula that employs the Z-score. Substituting the current values we get So, the 95% confidence interval is (-14.1, -10.7). Interpretation: We are 95% confidence interval is depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively the depressive symptoms after taking the new drug as compared to placebo is between 10.7 and 14.1 units (or alternatively taking ta the new drug as compared to placebo). Because we computed the differences by subtracting the scores after taking the placebo from the scores after taking the new drug and because higher scores after taking the placebo from the scores after taking the new drug and because higher scores after taking the placebo from the scores after taking the new drug and because higher scores aft taking the new drug as compared to placebo). Because the 95% confidence interval for the mean difference (in this case a significant improvement) in depressive symptom scores after taking the new drug as compared to placebo. Confidence Interval for Two Independent Samples, Dichotomous Outcome It is common to compare two independent groups with respect to the presence or absence of a dichotomous, the analysis involves comparing the proportions of successes between the two groups. There are several ways of comparing proportions in two independent groups. One can compute a risk difference, which is computed by taking the difference in means for a continuous outcome. The risk ratio (or relative risk) is another useful measure to compare proportions. Generally the reference group (e.g., unexposed persons, persons without a risk factor or persons assigned to the control group in a clinical trial setting) is considered in the denominator of the ratio. The risk ratio is a good measure of the strength of an effect, while the risk and, therefore provides an indication of how many people might benefit from an intervention. An odds ratio is the measure of association used in case-control studies. It is the ratio of the odds or disease in those with a risk factor compared to the odds of disease in those without the risk factor. When the outcome of interest is relatively uncommon (e.g., 30, use and use the z-table for standard normal distribution If n < 30, use the t-table with degrees of freedom (df)=n-1 Confidence interval for a proportion from one sample (p) with a dichotomous outcome Confidence interval for a risk ratio (RR) or prevalence ratio from two independent samples RR = p1/p2 Then take exp[lower limit of Ln(RR)] and exp[upper limit of Ln(RR)] to get the lower and upper limits of the confidence interval for RR. Confidence interval for RR. Confidence interval for OR. Note that this summary table only provides formulas for larger samples. As noted throughout the modules alternative formulas must be used for small samples. References Newcomb RG. Two-sided confidence intervals for the single proportion: Comparison of seven methods. Statistics in Medicine 1998;17(8): 857-872. StatXact version 7[©] 2006 by Cytel, Inc., Cambridge, MA. D'Agostino RB, Sullivan LM and Beiser A: Introductory Applied Biostatistics. Belmont, CA: Duxbury-Brooks/Cole; 2004 Rosner B. Fundamentals of Biostatistics. Belmont, CA: Duxbury-Brooks/Cole; 2006. Agresti A. Categorical Data Analysis 2nd ed., New York: John Wiley & Sons, 2002. Rothman KJ and Greenland S. Modern Epidemiology 2nd ed., Philadelphia. Lippincott-Raven Publishers, 1998 Solutions to Selected Problems the table above, what is the 90% confidence interval for BMI? Solution: Once again, the sample size was 10, so we go to the t-table and use the row with 10 minus 1 degrees of freedom). But now you want a 90% confidence interval, so you would use the column with a two-tailed probability of 0.10. Looking down to the row for Page 4 The table below, from the 5th examination of the Framingham Offspring cohort, shows the number of men and women found with or without cardiovascular disease (CVD). Estimate the prevalence of CVD in men using a 95% confidence interval. Free of CVD Prevalent CVD Total Men 1,548 244 1,792 Women 1,872 135 2,007 Total 3,420 379 3,799 The prevalence of cardiovascular disease (CVD) among men is 244/1792=0.1362. The sample size is large and satisfies the requirement that the number of failures is greater than 5. Therefore, the following formula can be used again. Substituting, we get So, the 95% confidence interval is (0.120, the new treatment group is group 1, and the standard treatment group is group 2. Therefore, 24% more patients reported a meaningful reduction in pain with the new drug compared to the standard pain reliever. Since there are more than 5 events (pain relief) and non-events (absence of pain relief) in each group, the large sample formula using the z-score can be used. Substituting we get This further simplifies to So, the 96% confidence interval for this risk difference is (0.06, 0.42). Interpretation: Our best estimate is an increase of 24% in pain relief with the new treatment, and with 95% confidence, the risk difference is between 6% and 42%. Since the 95% confidence interval does not contain developed pain reliever for patients following joint replacement surgery. Using the data in the table below, compute the point estimate for the relative risk, and interpret your findings in words. Treatment Group n # with Reduction of 3+ Points Proportion with Reduction of 3+ Points New Pain Reliever 50 23 0.46 Standard Pain Reliever 50 23 0.46 Standard Pain Reliever 50 21 0.22 The point estimate for the relative risk is Patients receiving the new drug are 2.09 times more likely to report a meaningful reduction in pain compared to those receiving the standard pain reliever. The 95% confidence interval for ln(RR). To compute the upper and lower limits for the confidence interval for RR we must find the antilog using the (exp) function: Therefore, we are 95% confident that patients receiving the new pain reliever are for patients receiving new pain reliever as compared to patients receiving standard pain reliever, and the 95% confidence interval for the odds ratio. Treatment Group n # with Reduction of 3+ Points New Pain Reliever 50 23 0.46 Standard Pain Reliever 50 11 0.22 It is easier to solve this problem if the information is organized in a contingency table in this way: Pain Relief 3+ Less Relief New Drug 23 27 Standard Drug 11 39 Odds of pain relief 3+ with standard drug = 11/39 = 0.2821 Odds Ratio = 0.8519 / 0.2821 = 3.02 To compute the 95% confidence interval for the odds ratio we use Substituting we get Since we used the log (Ln), we now need to take the antilog to get the limits of the confidente interval. The point estimate of the odds ratio is OR=3.2, and we are 95% confident that the true odds ratio lies between 1.27 and 7.21. This is statistically significant because the 95% confidence interval does not include the null value (OR=1.0). Note also that the odds ratio for the same problem. For mathematical reasons the odds ratio tends to exaggerate associates when the outcome is more common. Answer to Pain Reliever for patients following joint replacement surgery. Using the data in the table below, compute the point estimate for the relative risk for achieving the standard pain relief, comparing those receiving the standard pain relief. Then compute the 95% confidence interval for the relative risk, and interpret your findings in words. Treatment Group n # with Reduction of 3+ Points Proportion with Reduction of 3+ Points New Pain Reliever 50 23 0.46 Standard Pain Reliever 50 11 0.22

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