Medical Statistics

A Guide to Data Analysis and Critical Appraisal

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Foreword by Martin Bland, Professor of Health Statistics at the University of York

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Foreword

Most research in health care is not done by professional researchers, but by health-care practitioners. This is very unusual; agricultural research is not done by farmers, and building research is not done by bricklayers. I am told that it is positively frowned upon for social workers to carry out research, when they could be solving the problems of their clients. Practitioner-led research comes about, in part, because only clinicians, of whatever professional background, have access to the essential research material, patients. But it also derives from a long tradition, in medicine for example, that it is part of the role of the doctor to add to medical knowledge. It is impossible to succeed in many branches of medicine without a few publications in medical journals. This tradition is not confined to medicine. Let us not forget that Florence Nightingale was known as 'the Passionate Statistician' and her greatest innovation was that she collected data to evaluate her nursing practice. (She was the first woman to become a fellow of the Royal Statistical Society and is a heroine to all thinking medical statisticians.)

There are advantages to this system, especially for evidence-based practice. Clinicians often have direct experience of research as participants and are aware of some of its potential and limitations. They can claim ownership of the evidence they are expected to apply. The disadvantage is that health-care research is often done by people who have little training in how to do it and who have to do their research while, at the same time, carrying on a busy clinical practice. Even worse, research is often a rite of passage: the young researcher carries out one or two projects and then moves on and does not do research again. Thus there is a continual stream of new researchers, needing to learn quickly how to do it, yet there is a shortage of senior researchers to act as mentors. And research is not easy. When we do a piece of research, we are doing something no one has done before. The potential for the explorer to make a journey which leads nowhere is great.

The result of practitioner-led research is that much of it is of poor quality, potentially leading to false conclusions and sub-optimal advice and treatment for patients. People can die. It is also extremely wasteful of the resources of institutions which employ the researchers and their patients. From the researchers' point of view, reading the published literature is difficult because the findings of others cannot be taken at face value and each paper must be read critically and in detail. Their own papers are often rejected and even once published they are open to criticism because the most careful refereeing procedures will not correct all the errors.

When researchers begin to read the research literature in their chosen field, one of the first things they will discover is that knowledge of statistics is essential. There is no skill more ubiquitous in health-care research. Several of my former medical students have come to me for a bit of statistical advice, telling me how they now wished they had listened more when I taught them. Well, I wish they had, too, but it would not have been enough. Statistical knowledge is very hard to gain; indeed, it is one of the hardest subjects there is, but it is also very hard to retain. Why is it that I can remember the lyrics (though not, my family assures me, the tunes) of hundreds of pop songs of my youth, but not the details of any statistical method I have not applied in the last month? And I spend much of my time analysing data.

What the researchers need is a statistician at their elbow, ready to answer any questions that arise as they design their studies and analyse their data. They are so hard to find. Even one consultation with a statistician, if it can be obtained at all, may involve a wait for weeks. I think that the most efficient way to improve health-care research would be to train and employ, preferably at high salaries, large numbers of statisticians to act as collaborators. (Incidentally, statisticians should make the ideal collaborators, because they will not care about the research question, only about how to answer it, so there is no risk of them stealing the researcher's thunder.) Until that happy day dawns, statistical support will remain as hard to find as an honest politician. This book provides the next best thing.

The authors have great experience of research collaboration and support for researchers. Jenny Peat is a statistician who has co-authored more than a hundred health research papers. She describes herself as a 'research therapist', always ready to treat the ailing project and restore it to publishable health. Belinda Barton brings the researcher's perspective, coming into health research from a background in psychology. Their practical experience fills these pages. The authors guide the reader through all the methods of statistical analysis commonly found in the health-care literature. They emphasise the practical details of calculation, giving detailed guidance as to the computation of the methods they describe using the popular program SPSS. They rightly stress the importance of the assumptions of methods, including those which statisticians often forget to mention, such as the independence of observations. Researchers who follow their advice should not be told by statistical referees that their analyses are invalid. Peat and Barton close each chapter with a list of things to watch out for when reading papers which report analysis using the methods they have just described. Researchers will also find these invaluable as checklists to use when reading over their own work.

I recently remarked that my aim for my future career is to improve the quality of health-care research. 'What, worldwide?', I was asked. Of course, why limit ourselves? I think that this book, coming from the other side of the world from me, will help bring that target so much closer.

Martin Bland,
Professor of Health Statistics, University of York,
August 2004

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Introduction

Statistical thinking will one day be as necessary a qualification for efficient citizenship as the ability to read and write.
H.G. WELLS

Anyone who is involved in medical research should always keep in mind that science is a search for the truth and that, in searching for the truth, there is no room for bias or inaccuracy in statistical analyses or their interpretation.

Analysing the data and interpreting the results are the most exciting stages of a research project because these provide the answers to the study questions. However, data analyses must be undertaken in a careful and considered way by people who have an inherent knowledge of the nature of the data and of their interpretation. Any errors in statistical analyses will mean that the conclusions of the study may be incorrect[1]. As a result, many journals ask reviewers to scrutinise the statistical aspects of submitted articles and many research groups include statisticians who direct the data analyses. Analysing data correctly and including detailed documentation so that others can reach the same conclusions are established markers of scientific integrity. Research studies that are conducted with integrity bring personal pride, contribute to a successful track record and foster a better research culture.

In this book, we provide a guide to conducting and interpreting statistics in the context of how the participants were recruited, how the study was designed, what types of variables were used, what effect size was found and what the *P* values mean. We also guide researchers through the processes of selecting the correct statistic and show how to report results for publication or presentation. We have included boxes of SPSS and SigmaPlot commands in which we show the window names with the commands indented. We do not always include all of the tables from the SPSS output but only the most relevant information. In our examples, we use SPSS version 11.5 and SigmaPlot version 8 but the messages apply equally well to other versions and other statistical packages.

We have separated the chapters into sections according to whether data are continuous or categorical in nature because this classification is fundamental to selecting the correct statistics. At the end of the book, there is a glossary of terms as an easy reference that applies to all chapters and a list of useful Web sites. We have written this book as a guide from first principles with explanations of assumptions and how to interpret results. We hope that both novice statisticians and seasoned researchers will find this book a helpful guide to working with their data.

In this era of evidence-based health care, both clinicians and researchers need to critically appraise the statistical aspects of published articles in order to judge the implications and reliability of reported results. Although the peer review process goes a long way to improving the standard of research literature, it is essential to have the skills to decide whether published results are credible and therefore have implications for current clinical practice or future research directions. We have therefore included critical appraisal guidelines at the end of each chapter to help researchers to review the reporting of results from each type of statistical test.

There is a saying that 'everything is easy when you know how' – we hope that this book will provide the 'know how' and make statistical analysis and critical appraisal easy for all researchers and health-care professionals.

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CHAPTER 1
Data management: preparing to analyse the data

There are two kinds of statistics, the kind you look up and the kind you make up.
REX STOUT

Objectives

The objectives of this chapter are to explain how to:

- create a database that will facilitate straightforward statistical analyses
- devise a data management plan
- ensure data quality
- move data between electronic spreadsheets
- manage and document research data
- select the correct statistical test
- critically appraise the quality of reported data analyses

Creating a database

Creating a database in SPSS and entering the data is a relatively simple process. First, a new file can be opened using the *File* → *New* →*Data* commands at the top left hand side of the screen. The SPSS data editor has two different screens called the Data View and Variable View screens. You can easily move between the two views by clicking on the tabs at the bottom left hand side of the screen.

Before entering data in Data View, the characteristics of each variable need to be defined in Variable View. In this screen, details of the variable names, variable types and labels are stored. Each row in Variable View represents a new variable. To enter a variable name, simply type the name into the first field and default settings will appear for the remaining fields. The Tab or the arrow keys can be used to move across the fields and change the default settings. The settings can be changed by pulling down the drop box option that appears when you double click on the domino on the right hand side of each cell. In most cases, the first variable in a data set will be a unique identification number for each participant. This variable is invaluable for selecting or tracking particular participants during the data analysis process.

The Data View screen, which displays the data values, shows how the data have been entered. This screen is similar to many other spreadsheet packages. A golden rule of data entry is that the data for each participant should occupy one row only in the spreadsheet. Thus, if follow up data have been collected from the participants on one or more occasions, the participants' data should be an extension of their baseline data row and not a new row in the spreadsheet. An exception to this rule is for studies in which controls are matched to cases by characteristics such as gender or age or are selected as the unaffected sibling or a nominated friend of the case and therefore the data are naturally paired. The data from matched case-control studies are used as pairs in the statistical analyses and therefore it is important that matched controls are not entered on a separate row but are entered into the same row in the spreadsheet as their matched case. This method will inherently ensure that paired or matched data are analysed correctly and that the assumptions of independence that are required by many statistical tests are not violated. Thus, in Data View, each column represents a separate variable and each row represents a single participant, or a single pair of participants in a matched case-control study, or a single participant with follow-up data.

Unlike Excel, it is not possible to hide rows or columns in either Variable View or Data View in SPSS. Therefore, the order of variables in the spreadsheet should be considered before the data are entered. The default setting for the lists of variables in the drop down boxes that are used when running the statistical analyses are in the same order as the spreadsheet. It is more efficient to place variables that are likely to be used most often at the beginning of the data file and variables that are going to be used less often at the end.

After the information for each variable has been defined in Variable View, the data can be entered in the Data View screen. Before entering data, the details entered in the Variable View can be saved using the commands shown in Box 1.1.

Box 1.1 SPSS commands for saving a file

SPSS Commands

Untitled – SPSS Data Editor

    File → Save As

Save Data As

    Enter the name of the file in File name

Click on Save

After saving the file, the name of the file will replace the word *Untitled* at the top left hand side of the Data View screen. Data entered into the Variable View can be also saved using the commands shown in Box 1.1. It is not possible to close a data file in SPSS Data Editor. The file can only be closed by opening a new data file or by exiting the SPSS program.

Variable names

If data are entered in Excel or Access before being exported to SPSS, it is a good idea to use variable names that are accepted by SPSS to avoid having to rename the variables. In SPSS, each variable name has a maximum of eight characters and must begin with an alphabetic character. In addition, each variable name must be unique. Some symbols such as @, # or $ can be used in variable names but other symbols such as %, > and punctuation marks are not accepted. Also, SPSS is not case sensitive and capital letters will be converted to lower case letters.

Types of variables

Before conducting any statistical tests, a formal, documented plan that includes a list of questions to be answered and identifies the variables that will be used should be drawn up. For each question, a decision on how each variable will be used in the analyses, for example as a continuous or categorical variable or as an outcome or explanatory variable, will need to be made.

Table 1.1 shows a classification system for variables and how the classification influences the presentation of results. A common error in statistical analyses is to misclassify the outcome variable as an explanatory variable or to misclassify an intervening variable as an explanatory variable. It is important that an intervening variable, which links the explanatory and outcome variable because it is directly on the pathway to the outcome variable, is not treated as an independent explanatory variable in the analyses[1]. It is also important that an alternative outcome variable is not treated as an independent risk factor. For example, hay fever cannot be treated as an independent risk factor for asthma because it is a symptom that is a consequence of the same allergic developmental pathway.

Table 1.1 Names used to identify variables

Variable name	Alternative name/s	Axis for plots, data analysis and tables
Outcome variables	Dependent variables (DVs)	*y*-axis, columns
Intervening variables	Secondary or alternative outcome variables	*y*-axis, columns
Explanatory variables	Independent variables (IVs) Risk factors Exposure variables Predictors	*x*-axis, rows

In part, the classification of variables depends on the study design. In a case-control study in which disease status is used as the selection criterion, the explanatory variable will be the presence or absence of disease and the outcome variable will be the exposure. However, in most other observational and experimental studies such as clinical trials, cross-sectional and cohort studies, the disease will be the outcome and the exposure will be the explanatory variable.

In SPSS, the measurement level of the variable can be classified as nominal, ordinal or scale under the *Measure* option in Variable View. The measurement scale used determines each of these classifications. Nominal scales have no order and are generally category labels that have been assigned to classify items or information. For example, variables with categories such as male or female, religious status or place of birth are nominal scales. Nominal scales can be string (alphanumeric) values or numeric values that have been assigned to represent categories, for example 1 = male and 2 = female.

Values on an ordinal scale have a logical or ordered relationship across the values and it is possible to measure some degree of difference between categories. However, it is usually not possible to measure a specific amount of difference between categories. For example, participants may be asked to rate their overall level of stress on a five-point scale that ranges from no stress, mild stress, moderate stress, severe stress to extreme stress. Using this scale, participants with severe stress will have a more serious condition than participants with mild stress, although recognising that self-reported perception of stress may be quite subjective and is unlikely to be standardised between participants. With this type of scale, it is not possible to say that the difference between mild and moderate stress is the same as the difference between moderate and severe stress. Thus, information from these types of variables has to be interpreted with care.

Variables with numeric values that are measured by an interval or ratio scale are classified as scale variables. On an interval scale, one unit on the scale represents the same magnitude across the whole scale. For example, Fahrenheit is an interval scale because the difference in temperature between 10 °F and 20 °F is the same as the difference in temperature between 40 °F and 50 °F. However, interval scales have no true zero point. For example, 0 °F does not indicate that there is no temperature. Because interval scales have an arbitrary rather than a true zero point, it is not possible to compare ratios.

A ratio scale has the same properties as nominal, ordinal, and interval scales, but has a true zero point and therefore ratio comparisons are valid. For example, it is possible to say that a person who is 40 years old is twice as old as a person who is 20 years old and that a person is 0 year old at birth. Other common ratio scales are length, weight and income.

While variables in SPSS can be classified as scale, ordinal or nominal values, a more useful classification for variables when deciding how to analyse data is as categorical variables (ordered or non-ordered) or continuous variables.

These classifications are essential for selecting the correct statistical test to analyse the data. However, these classifications are not provided in Variable View by SPSS.

The file **surgery.sav**, which contains the data from 141 babies who underwent surgery at a paediatric hospital, can be opened using the *File* → *Open* → *Data* commands. The classification of the variables as shown by SPSS and the classifications that are needed for statistical analysis are shown in Table 1.2.

Table 1.2 Classification of variables in the file surgery.sav

Variable label	Type	SPSS measure	Classification for analysis decisions
ID	Numeric	Scale	Not used in analyses
Gender	String	Nominal	Categorical/non-ordered
Place of birth	String	Nominal	Categorical/non-ordered
Birth weight	Numeric	Scale	Continuous
Gestational age	Numeric	Ordinal	Continuous
Length of stay	Numeric	Scale	Continuous
Infection	Numeric	Scale	Categorical/non-ordered
Prematurity	Numeric	Scale	Categorical/non-ordered
Procedure performed	Numeric	Nominal	Categorical/non-ordered

Obviously, categorical variables have discrete categories, such as male and female, and continuous variables are measured on a scale, such as height which is measured in centimetres. Categorical values can be non-ordered, for example gender which is coded as 1 = male and 2 = female and place of birth which is coded as 1 = local, 2 = regional and 3 = overseas. Categorical variables can also be ordered, for example, if the continuous variable length-of-stay was re-coded into categories of 1 = 1–10 days, 2 = 11–20 days, 3 = 21–30 days and 4 = >31 days, there is a progression in magnitude of length of stay.

Data organisation and data management

Prior to beginning statistical analysis, it is essential to have a thorough working knowledge of the nature, ranges and distributions of each variable. Although it may be tempting to jump straight into the analyses that will answer the study questions rather than spend time obtaining seemingly mundane descriptive statistics, a working knowledge of the data often saves time in the end by avoiding analyses having to be repeated for various reasons.

It is important to have a high standard of data quality in research databases at all times because good data management practice is a hallmark of scientific integrity. The steps outlined in Box 1.2 will help to achieve this.

Box 1.2 Data organisation

The following steps ensure good data management practices:

- Use numeric codes for categorical data where possible
- Choose appropriate variable names and labels to avoid confusion across variables
- Check for duplicate records and implausible data values
- Make corrections
- Archive a back-up copy of the data set for safe keeping
- Limit access to sensitive data such as names and addresses in working files

It is especially important to know the range and distribution of each variable and whether there are any outlying values or outliers so that the statistics that are generated can be explained and interpreted correctly. Describing the characteristics of the sample also allows other researchers to judge the generalisability of the results. A considered pathway for data management is shown in Box 1.3.

Box 1.3 Pathway for data management before beginning statistical analysis

The following steps are essential for efficient data management:

- Obtain the minimum and maximum values and the range of each variable
- Conduct frequency analyses for categorical variables
- Use box plots, histograms and other tests to ascertain normality of continuous variables
- Identify and deal with missing values and outliers
- Re-code or transform variables where necessary
- Re-run frequency and/or distribution checks
- Document all steps in a study handbook

The study handbook should be a formal documentation of all of the study details that is updated continuously with any changes to protocols, management decisions, minutes of meetings, etc. This handbook should be available for anyone in the team to refer to at any time to facilitate considered data collection and data analysis practices. Suggested contents of data analysis log sheets that could be kept in the study handbook are shown in Box 1.4.

Data analyses must be planned and executed in a logical and considered sequence to avoid errors or misinterpretation of results. In this, it is important that data are treated carefully and analysed by people who are familiar with their content, their meaning and the interrelationship between variables.

Box 1.4 Data analysis log sheets

Data analysis log sheets should contain the following information:

- Title of proposed paper, report or abstract
- Author list and author responsible for data analyses and documentation
- Specific research questions to be answered or hypotheses tested
- Outcome and explanatory variables to be used
- Statistical methods
- Details of database location and file storage names
- Journals and/or scientific meetings where results will be presented

Before beginning any statistical analyses, a data analysis plan should be agreed upon in consultation with the study team. The plan can include the research questions that will be answered, the outcome and explanatory variables that will be used, the journal where the results will be published and/or the scientific meeting where the findings will be presented.

A good way to handle data analyses is to create a log sheet for each proposed paper, abstract or report. The log sheets should be formal documents that are agreed to by all stakeholders and that are formally archived in the study handbook. When a research team is managed efficiently, a study handbook is maintained that has up to date documentation of all details of the study protocol and the study processes.

Documentation

Documentation of data analyses, which allows anyone to track how the results were obtained from the data set collected, is an important aspect of the scientific process. This is especially important when the data set will be accessed in the future by researchers who are not familiar with all aspects of data collection or the coding and recoding of the variables.

Data management and documentation are relatively mundane processes compared to the excitement of statistical analyses but, nevertheless, are essential. Laboratory researchers document every detail of their work as a matter of course by maintaining accurate laboratory books. All researchers undertaking clinical and epidemiological studies should be equally diligent and document all of the steps taken to reach their conclusions.

Documentation can be easily achieved by maintaining a data management book for each data analysis log sheet. In this, all steps in the data management processes are recorded together with the information of names and contents of files, the coding and names of variables and the results of the statistical analyses. Many funding bodies and ethics committees require that all steps in data analyses are documented and that in addition to archiving the data, both the data sheets and the records are kept for 5 or sometimes 10 years after the results are published.

In SPSS, the file details, variable names, details of coding etc. can be viewed by clicking on Variable View. Documentation of the file details can be obtained and printed using the commands shown in Box 1.5. The output can then be stored in the study handbook or data management log book.

Box 1.5 SPSS commands for printing file information

SPSS Commands

```
Untitled – SPSS Data Editor
        File → Open Data
                surgery.sav
        Utilities → File Info
Output – SPSS Viewer
        File → Print
        Click OK
        (to view File Info on screen, double click on the output on the RHS and use
          the down arrow key to scroll down)
```

The following output is produced:

```
              List of variables on the working file
Name                                                              Position

ID        ID                                                             1
          Measurement Level: Scale
          Column Width: 8  Alignment: Right
          Print Format: F5
          Write Format: F5

GENDER    Gender                                                         2
          Measurement Level: Nominal
          Column Width: 5  Alignment: Left
          Print Format: A5
          Write Format: A5

PLACE     Place of birth                                                 3
          Measurement Level: Nominal
          Column Width: 5  Alignment: Left
          Print Format: A5
          Write Format: A5

BIRTHWT   Birth weight                                                   4
          Measurement Level: Scale
          Column Width: 8  Alignment: Right
          Print Format: F8
          Write Format: F8

GESTATIO  Gestational age                                     5
          Measurement Level: Ordinal
          Column Width: 8  Alignment: Right
          Print Format: F8.1
          Write Format: F8.1

LENGTHST  Length of stay                                      6
          Measurement Level: Scale
          Column Width: 8  Alignment: Right
          Print Format: F8
          Write Format: F8

INFECT    Infection                                           7
          Measurement Level: Scale
          Column Width: 8  Alignment: Right
          Print Format: F8
          Write Format: F8

          Value    Label

              1    No
              2    Yes

PREMATUR  Prematurity                                         8
          Measurement Level: Scale
          Column Width: 8  Alignment: Right
          Print Format: F8
          Write Format: F8

          Value    Label

              1    Premature
              2    Term

SURGERY   Procedure performed                                 9
          Measurement Level: Nominal
          Column Width: 8  Alignment: Right
          Print Format: F5
          Write Format: F5

          Value    Label

              1    Abdominal
              2    Cardiac
              3    Other
```

This file information can be directly printed from SPSS or exported from the SPSS output viewer into a word processing document using the commands shown in Box 1.6. From a word processing package, the information is easily printed and stored.

Box 1.6 SPSS commands for exporting file information into a word document

SPSS Commands

Output – SPSS Viewer
    Click on 'File Information' on the LHS of the screen
    File → Export
Export Output
    Use Browse to indicate the directory to save the file
    Click on File Type to show Word/RTF file (.doc)*
    Click OK

Importing data from Excel

Specialised programs are available for transferring data between different data entry and statistics packages (see Useful Web sites). Many researchers use Excel or Access for ease of entering and managing the data. However, statistical analyses are best executed in a specialist statistical package such as SPSS in which the integrity and accuracy of the statistics are guaranteed. Importing data into SPSS from Access is not a problem because Access 'talks' to SPSS so that data can be easily transferred between these programs. However, exporting data from Excel into SPSS requires a few more steps using the commands shown in Box 1.7.

Box 1.7 SPSS commands for opening an Excel data file

SPSS Commands

Untitled – SPSS Data Editor
    File → Open →Data
Open File
    Click on 'Files of type' to show 'Excel (.xls)'*
    Click on your Excel file
    Click Open
Opening Excel Data Source
    Click OK

The commands shown in Box 1.7 have the disadvantage that they convert numerical fields to string fields and may lose the integrity of any decimal places, etc. The data then have to be reformatted in SPSS, which is feasible for a limited number of variables but is a problem with larger data sets. As an alternative, the commands shown in Box 1.8 will transport data from Excel to SPSS more effectively. These commands take a little longer and require more patience, but the formatting of the data fields and the integrity of the database will be maintained in SPSS. For numeric values, blank cells in Excel or Access are converted to the system missing values, that is a full stop, in SPSS.

Box 1.8 SPSS commands for importing an Excel file

SPSS Commands

Untitled – SPSS Data Editor
    File → Open Database→New Query
Database Wizard
    Highlight Excel Files / Click Add Data Source
ODBC Data Source Administrator - User DSN
    Highlight Excel Files / Click Add
Create New Data Source
    Highlight Microsoft Excel Driver (.xls)*
    Click Finish
ODBC Microsoft Excel Setup
    Enter a new data name in Data Source Name (and description if required)
    Select Workbook
Select Workbook
    Highlight .xls file to import
    Click OK
ODBC Microsoft Excel Setup
    Click OK
ODBC Data Source Administrator - User DSN
    Click OK
Database Wizard
    Highlight new data source name (as entered above) / Click Next
    Click on items in Available Tables on the LHS and drag it across to the Retrieve Fields list on the RHS / Click Next / Click Next
    Step 5 of 6 will identify any variable names not accepted by SPSS (if names are rejected click on Result Variable Name and change the variable name)
    Click Next
    Click Finish

Once in the SPSS spreadsheet, features of the variables can be adjusted in Variable View, for example by changing the width and column length of string variables, entering the labels and values for categorical variables and checking that the number of decimal places is appropriate for each variable. Once data quality is ensured, a back up copy of the database should be archived at a remote site for safety. Few researchers ever need to resort to their archived copies but, when they do, they are an invaluable resource.

The spreadsheet that is used for data analyses should not contain any information that would contravene ethics guidelines by identifying individual participants. In the working data file, names, addresses, dates of birth and any other identifying information that will not be used in data analyses should be removed. Identifying information that is required can be re-coded and de-identified, for example, by using a unique numerical value that is assigned to each participant.

Missing values

Data values that have not been measured in some participants are called missing values. Missing values create pervasive problems in data analyses. The seriousness of the problem depends largely on the pattern of missing data, how much is missing, and why it is missing[2].

Missing values must be treated appropriately in analyses and not inadvertently included as data points. This can be achieved by proper coding that is recognised by the software as a system missing value. The most common character to indicate a missing value is a full stop. This is preferable to using the implausible value of 9 or 999 that has been commonly used in the past. If these values are not accurately defined as missing values, statistical programs can easily incorporate them into the analyses, thus producing erroneous results. Although these values can be predefined as system missing, this is an unnecessary process that is discouraged because it requires familiarity with the coding scheme and because the analyses will be erroneous if the missing values are inadvertently incorporated into the analyses.

For a full stop to be recognised as a system missing value, the variable must be formatted as numeric rather than a string variable. In the spreadsheet **surgery.sav**, the data for place of birth are coded as a string variable. The command sequences shown in Box 1.9 can be used to obtain frequency information of this variable:

Box 1.9 SPSS commands for obtaining frequencies

SPSS Commands

surgery – SPSS Data Editor

Analyze → Descriptive Statistics→Frequencies

Frequencies

Highlight 'Place of birth' and click into Variable(s)

Click OK

Frequency table

Place of Birth

		Frequency	Per cent	Valid per cent	Cumulative per cent
Valid	.	9	6.4	6.4	6.4
	L	90	63.8	63.8	70.2
	O	9	6.4	6.4	76.6
	R	33	23.4	23.4	100.0
	Total	141	100.0	100.0	

Since place of birth is coded as a string variable, the missing values are treated as valid values and included in the summary statistics of valid and cumulative percentages shown in the Frequency table. To remedy this, the syntax shown in Box 1.10 can be used to re-code place of birth from a string variable into a numeric variable.

Box 1.10 Recoding a variable into a different variable

SPSS Commands

surgery – SPSS Data Editor

    Transform → Recode → Into Different Variables

Recode into Different Variables

    Highlight 'Place of birth' and click into Input Variable → Output Variable
    Enter Output Variable Name as place2,
    Enter Output Variable Label as Place of birth recoded/ Click Change
    Click Old and New Values

Recode into Different Variables: Old and New Values

    Old Value→Value=L, New Value→Value=1/Click Add
    Old Value→Value=R, New Value→Value=2/Click Add
    Old Value→Value=O, New Value→Value=3/Click Add
    Click Continue

Recode into Different Variables

    Click OK (or 'Paste/Run→All')

The paste command is a useful tool to provide automatic documentation of any changes that are made. The paste screen can be saved or printed for documentation and future reference. Using the *Paste* command for the above re-code provides the following documentation.

```
RECODE
  place
  ('L'=1) ('R'=2) ('O'=3) INTO place2
  VARIABLE LABELS place2 'Place of birth recoded'.
EXECUTE .
```

After recoding, the value labels for the three new categories of place2 that have been created can be added in the Variable View window. In this case, place of birth needs to be defined as 1 = Local, 2 = Regional and 3 = Overseas. This can be added by clicking on the Values cell and then double clicking on the grey domino box on the right of the cell to add the value labels. Similarly, gender which is also a string variable can be re-coded into a numeric variable, gender2 with Male = 1 and Female = 2. After re-coding variables, it is important to also check whether the number of decimal places is appropriate. For categorical variables, no decimal places are required. For continuous variables, the number of decimal places must be the same as the number that the measurement was collected in.

A useful function in SPSS to repeat recently conducted commands is the *Dialog Recall* button. This button recalls the most recently used SPSS commands conducted. The *Dialog Recall* button is the fourth icon at the top left hand side of the Data View screen or the sixth icon in the top left hand side of the SPSS Output Viewer screen.

Using the *Dialog Recall* button to obtain *Frequencies* for place2, which is labelled Place of birth recoded, the following output is produced.

Frequencies

Place of Birth Recoded

		Frequency	Per cent	Valid per cent	Cumulative per cent
Valid	Local	90	63.8	68.2	68.2
	Regional	33	23.4	25.0	93.2
	Overseas	9	6.4	6.8	100.0
	Total	132	93.6	100.0	
Missing	System	9	6.4		
Total		141	100.0		

The frequencies in the table show that the recoding sequence was executed correctly. When the data are re-coded as numeric, the nine babies who have missing data for birthplace are correctly omitted from the valid and cumulative percentages.

When collecting data in any study, it is essential to have methods in place to prevent missing values in, say, at least 95% of the data set. Methods such as restructuring questionnaires in which participants decline to provide sensitive information or training research staff to check that all fields are complete at the point of data collection are invaluable in this process. In large epidemiological and longitudinal data sets, some missing data may be unavoidable. However, in clinical trials it may be unethical to collect insufficient information about some participants so that they have to be excluded from the final analyses.

If the number of missing values is small and the missing values occur randomly throughout the data set, the cases with missing values can be omitted from the analyses. This is the default option in most statistical packages and the main effect of this process is to reduce statistical power, that is the ability to show a statistically significant difference between groups when a clinically important difference exists. Missing values that are scattered randomly throughout the data are less of a problem than non-random missing values that can affect both the power of the study and the generalisability of the results. For example, if people in higher income groups selectively decline to answer questions about income, the distribution of income in the population will not be known and analyses that include income will not be generalisable to people in higher income groups.

In some situations, it may be important to replace a missing value with an estimated value that can be included in analyses. In longitudinal clinical trials, it has become common practice to use the last score obtained from the participant and carry it forward for all subsequent missing values. In other studies, a mean value (if the variable is normally distributed) or a median value (if the variable is non-normal distributed) may be used to replace missing values. These solutions are not ideal but are pragmatic in that they maintain the study power whilst reducing any bias in the summary statistics. Other more complicated methods for replacing missing values have been described[2].

Outliers

Outliers are data values that are surprisingly extreme when compared to the other values in the data set. There are two types of outliers: univariate outliers and multivariate outliers. A univariate outlier is a data point that is very different to the rest of the data for one variable. An outlier is measured by the distance from the remainder of the data in units of the standard deviation, which is a standardised measure of the spread of the data. For example, an IQ score of 150 would be a univariate outlier because the mean IQ of the population is 100 with a standard deviation of 15. Thus, an IQ score of 150 is 3.3 standard deviations away from the mean whereas the next closest value may be only 2 standard deviations away from the mean leaving a gap in the distribution of the data points.

A multivariate outlier is a case that is an extreme value on a combination of variables. For example, a boy aged 8 years with a height of 155 cm and a weight of 45 kg is very unusual and would be a multivariate outlier. It is important to identify values that are univariate and/or multivariate outliers because they can have a substantial influence on the distribution and mean of the variable and can influence the results of analyses and thus the interpretation of the findings.

Univariate outliers are easier to identify than multivariate outliers. For a continuously distributed variable with a normal distribution, about 99% of scores are expected to lie within 3 standard deviations above and below the mean value. Data points outside this range are classified as univariate outliers. Sometimes a case that is a univariate outlier for one variable will also be a univariate outlier for another variable. Potentially, these cases may be multivariate outliers. Multivariate outliers can be detected using statistics called leverage values or Cook's distances, which are discussed in Chapter 5, or Mahalanobis distances, which are discussed in Chapter 6.

There are many reasons why outliers occur. Outliers may be errors in data recording, incorrect data entry values that can be corrected or genuine values. When outliers are from participants from another population with different characteristics to the intended sample, they are called contaminants. This happens for example when a participant with a well-defined illness is inadvertently included as a healthy participant. Occasionally, outliers can be excluded from the data analyses on the grounds that they are contaminants or biologically implausible values. However, deleting values simply because they are outliers is usually unacceptable and it is preferable to find a way to accommodate the values without causing undue bias in the analyses.

Identifying and dealing with outliers is discussed further throughout this book. Whatever methods are used to accommodate outliers, it is important that they are reported so that the methods used and the generalisability of the results are clear.

Choosing the correct test

Selecting the correct test to analyse data depends not only on the study design but also on the nature of the variables collected. Tables 1.3–1.6 show the types of tests that can be selected based on the nature of variables. It is of paramount importance that the correct test is used to generate *P* values and to estimate the size of effect. Using an incorrect test will inviolate the statistical assumptions of the test and may lead to bias in the *P* values.

Table 1.3 Choosing a statistic when there is one outcome variable only

Type of variable	Number of times measured in each participant	Statistic	SPSS menu
Binary	Once	Incidence or prevalence and 95% confidence interval (95% CI)	Descriptive statistics; Frequencies
	Twice	McNemar's chi-square Kappa	Descriptive statistics; Crosstabs
Continuous	Once	Tests for normality	Non-parametric tests; 1 sample K-S Descriptive statistics; Explore
		One sample *t*-test	Compare means; One-sample *t*-test
		Mean, standard deviation (SD) and 95% CI	Descriptive statistics; Explore
		Median and inter-quartile (IQ) range	Descriptive statistics; Explore
	Twice	Paired *t*-test	Compare means; Paired-samples *t*-test
		Mean difference and 95% CI	Compare means; Paired-samples *t*-test
		Measurement error	Compare means; Paired-samples *t*-test
		Mean-versus-differences plot	Graphs; Scatter
		Intraclass correlation coefficient	Scale; Reliability Analysis
	Three or more	Repeated measures ANOVA	General linear model; Repeated measures

Table 1.4 Choosing a statistic when there is one outcome variable and one explanatory variable

Type of outcome variable	Type of explanatory variable	Number of levels of the categorical variable	Statistic	SPSS menu
Categorical	Categorical	Both variables are binary	Chi-square	Descriptive statistics; Crosstabs
			Odds ratio or relative risk	Descriptive statistics; Crosstabs
			Logistic regression	Regression; Binary logistic
			Sensitivity and specificity	Descriptive statistics; Crosstabs
			Likelihood ratio	Descriptive statistics; Crosstabs
Categorical	Categorical	At least one of the variables has more than two levels	Chi-square	Descriptive statistics; Crosstabs
			Chi-square trend	Descriptive statistics; Crosstabs
			Kendall's correlation	Correlate; Bivariate
Categorical	Continuous	Categorical variable is binary	ROC curve	Graphs; ROC curve
			Survival analyses	Survival; Kaplan-Meier
Categorical	Continuous	Categorical variable is multi-level and ordered	Spearman's correlation coefficient	Correlate; Bivariate
Continuous	Categorical	Explanatory variable is binary	Independent samples *t*-test	Compare means; Independent-samples *t*-test
			Mean difference and 95% CI	Compare means; Independent-samples *t*-test
Continuous	Categorical	Explanatory variable has three or more categories	Analysis of variance	Compare means; One-way ANOVA
Continuous	Continuous	No categorical variables	Regression	Regression; Linear
			Pearson's correlation	Correlate; Bivariate

Table 1.5 Choosing a statistic for one or more outcome variables and more than one explanatory variable

Type of outcome variable/s	Type of explanatory variable/s	Number of levels of categorical variable	Statistic	SPSS menu
Continuous—only one outcome	Both continuous and categorical	Categorical variables are binary	Multiple regression	Regression; Linear
Continuous—only one outcome	Categorical	At least one of the explanatory variables has three or more categories	Two-way analysis of variance	General linear model; Univariate
Continuous—only one outcome	Both continuous and categorical	One categorical variable has two or more levels	Analysis of covariance	General linear model; Univariate
Continuous—outcome measured more than once	Both continuous and categorical	Categorical variables can have two or more levels	Repeated measures analysis of variance Auto-regression	General linear model; Repeated measures Times series; Auto-regression
No outcome variable	Both continuous and categorical	Categorical variables can have two or more levels	Factor analysis	Data reduction: Factor

Table 1.6 Parametric and non-parametric equivalents

Parametric test	Non-parametric equivalent	SPSS menu
Mean and standard deviation	Median and inter-quartile range	Descriptive statistics; Explore
Pearson's correlation coefficient	Spearman's or Kendall's correlation coefficient	Correlate; Bivariate
One sample sign test	Sign test	SPSS does not provide this option but a sign test can be obtained by computing a new constant variable equal to the test value (e.g. 0 or 100) and using non-parametric test; 2 related samples with the outcome and computed variable as the pair
Two sample *t*-test	Wilcoxon rank sum test	Non-parametric tests; 2 related samples
Independent *t*-test	Mann-Whitney U or Wilcoxon Rank Sum test	Non-parametric tests; 2 independent samples
Analysis of variance	Mann-Whitney U test	Non-parametric tests; K independent samples
Repeated measures analysis of variance	Friedmans ANOVA test	Nonparametric tests; K independent samples

Sample size requirements

The sample size is one of the most critical issues in designing a research study because it affects all aspects of interpreting the results. The sample size needs to be large enough so that a definitive answer to the research question is obtained. This will help to ensure generalisability of the results and precision around estimates of effect. However, the sample has to be small enough so that the study is practical to conduct. In general, studies with a small sample size, say with less than 30 participants, can usually only provide imprecise and unreliable estimates.

Box 1.11 provides a definition of type I and type II errors and shows how the size of the sample can contribute to these errors, both of which have a profound influence on the interpretation of the results.

In each chapter of this book, the implications of interpreting the results in terms of the sample size of the data set and the possibilities of type I and type II errors in the results will be discussed.

Golden rules for reporting numbers

Throughout this book the results are presented using the rules that are recommended for reporting statistical analyses in the literature[3–5]. Numbers are usually presented as digits except in a few special circumstances as indicated

Box 1.11 Type I and type II errors

Type I errors

- are false positive results
- occur when a statistical significant difference between groups is found but no clinically important difference exists
- the null hypothesis is rejected in error

Type II errors

- are false negative results
- a clinical important difference between groups does exist but does not reach statistical significance
- the null hypothesis is accepted in error
- usually occur when the sample size is small

in Table 1.7. When reporting data, it is important not to imply more precision than actually exists, for example by using too many decimal places. Results should be reported with the same number of decimal places as the measurement, and summary statistics should have no more than one extra decimal place. A summary of the rules for reporting numbers and summary statistics is shown in Table 1.7.

Table 1.7 Golden rules for reporting numbers

Rule	Correct expression
In a sentence, numbers less than 10 are words	In the study group, eight participants did not complete the intervention
In a sentence, numbers 10 or more are numbers	There were 120 participants in the study
Use words to express any number that begins a sentence, title or heading. Try and avoid starting a sentence with a number	Twenty per cent of participants had diabetes
Numbers that represent statistical or mathematical functions should be expressed in numbers	Raw scores were multiplied by 3 and then converted to standard scores
In a sentence, numbers below 10 that are listed with numbers 10 and above should be written as a number	In the sample, 15 boys and 4 girls had diabetes
Use a zero before the decimal point when numbers are less than 1	The *P* value was 0.013

Continued

Rule	Correct expression
Do not use a space between a number and its per cent sign	In total, 35% of participants had diabetes
Use one space between a number and its unit	The mean height of the group was 170 cm
Report percentages to only one decimal place if the sample size is larger than 100	In the sample of 212 children, 10.4% had diabetes
Report percentages with no decimal places if the sample size is less than 100	In the sample of 44 children, 11% had diabetes
Do not use percentages if the sample size is less than 20	In the sample of 18 children, 2 had diabetes
Do not imply greater precision than the measurement instrument	Only use one decimal place more than the basic unit of measurement when reporting statistics (means, medians, standard deviations, 95% confidence interval, inter-quartile ranges, etc.) e.g. mean height was 143.2 cm
For ranges use 'to' or a comma but not '-' to avoid confusion with a minus sign. Also use the same number of decimal places as the summary statistic	The mean height was 162 cm (95% CI 156 to 168) The mean height was 162 cm (95% CI 156, 168) The median was 0.5 mm (inter-quartile range −0.1 to 0.7) The range of height was 145 to 170 cm
P values between 0.001 and 0.05 should be reported to three decimal places	There was a significant difference in blood pressure between the two groups ($t = 3.0$, $df = 45$, $P = 0.004$)
P values shown on output as 0.000 should be reported as <0.0001	Children with diabetes had significantly lower levels of insulin than control children without diabetes ($t = 5.47$, $df = 78$, $P < 0.0001$)

Formatting the output

There are many output formats available in SPSS. The format of the frequencies table obtained previously can easily be changed by double clicking on the table and using the commands *Format* → *TableLooks*. To obtain the output in the format below, which is a classical academic format with no vertical lines and minimal horizontal lines that is used by many journals, highlight Academic 2 under *TableLooks Files* and click OK. The column widths and other features can also be changed using the commands *Format* → *Table Properties*. By clicking on the table and using the commands *Edit* → *Copy objects*, the table can be copied and pasted into a word file.

Place of Birth Recoded

		Frequency	Per cent	Valid per cent	Cumulative per cent
Valid	Local	90	63.8	68.2	68.2
	Regional	33	23.4	25.0	93.2
	Overseas	9	6.4	6.8	100.0
	Total	132	93.6	100.0	
Missing	System	9	6.4		
Total		141	100.0		

SPSS help commands

SPSS has two levels of extensive help commands. By using the commands *Help → Topics → Index*, the index of help topics appears in alphabetical order. By typing in a keyword, followed by enter, a topic can be displayed. Listed under the Help command is also Tutorial, which is a guide to using SPSS, and Statistics Coach, which is a guide to selecting the correct test to use.

There is also another level of help that explains the meaning of the statistics shown in the output. For example, help can be obtained for the above frequencies table by doubling clicking on the left hand mouse button to outline the table with a hatched border and then single clicking on the right hand mouse button on any of the statistics labels. This produces a dialog box with *What's This?* at the top. Clicking on *What's This?* provides an explanation of the highlighted statistical term. Clicking on *Cumulative Percent* gives the explanation that this statistic is the per cent of cases with non-missing data that have values less than or equal to a particular value.

Notes for critical appraisal

When critically appraising statistical analyses reported in the literature, that is when applying the rules of science to assess the validity of the results from a study, it is important to ask the questions shown in Box 1.12. Studies in which

Box 1.12 Questions for critical appraisal

Answers to the following questions are useful for checking the integrity of statistical analyses:

- Have details of the methods and statistical packages used to analyse the data been reported?
- Are the variables classified correctly as outcome and explanatory variables?
- Are any intervening or alternative outcome variables mistakenly treated as explanatory variables?
- Are missing values and outliers treated appropriately?
- Is the sample size large enough to avoid type II errors?

outliers are treated inappropriately, in which the quality of the data is poor or in which an incorrect statistical test has been used are likely to be biased and to lack scientific merit.

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CHAPTER 2

Continuous variables: descriptive statistics

It is wonderful to be in on the creation of something, see it used, and then walk away and smile at it.

LADY BIRD JOHNSON, U.S. FIRST LADY

Objectives

The objectives of this chapter are to explain how to:

- test whether a continuous variable has a normal distribution
- decide whether to use a parametric or non-parametric test
- present summary statistics for continuous variables
- decide whether parametric tests have been used appropriately in the literature

Before beginning statistical analyses of a continuous variable, it is essential to examine the distribution of the variable for skewness (tails), kurtosis (peaked or flat distribution), spread (range of the values) and outliers (data values separated from the rest of the data). If a variable has significant skewness or kurtosis or has univariate outliers, or any combination of these, it will not be normally distributed. Information about each of these characteristics determines whether parametric or non-parametric tests need to be used and ensures that the results of the statistical analyses can be accurately explained and interpreted. A description of the characteristics of the sample also allows other researchers to judge the generalisability of the results. A typical pathway for beginning the statistical analysis of continuous data variables is shown in Box 2.1.

Box 2.1 Data analysis pathway for continuous variables

The pathway for conducting the data analysis of continuous variables is as follows:

- conduct distribution checks
- transform variables with non-normal distributions or re-code into categorical variables, for example quartiles or quintiles
- re-run distribution checks for transformed variables
- document all steps in the study handbook

Statistical tests can be either parametric or non-parametric. Parametric tests are commonly used when a continuous variable is normally distributed. In general, parametric tests are preferable to non-parametric tests because a larger variety of tests are available and, as long as the sample size is not very small, they provide approximately 5% more power than rank tests to show a statistically significant difference between groups[1]. Non-parametric tests can be a challenge to present in a clear and meaningful way because summary statistics such as ranks are less familiar to many people than summary statistics from parametric tests. Summary statistics from parametric tests such as means and standard deviations are always more readily understood and more easily communicated than the equivalent rank statistics from non-parametric tests.

The pathway for the analysis of continuous variables is shown in Figure 2.1.

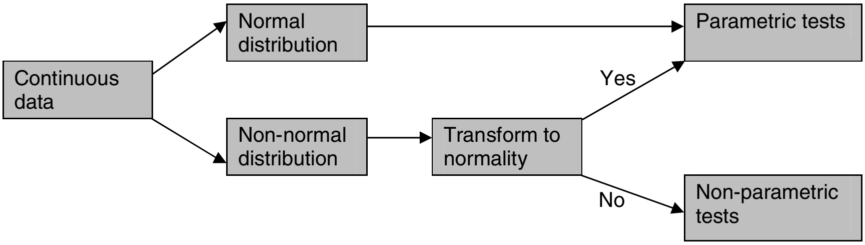


Figure 2.1 Pathway for the analysis of continuous variables.

Skewness, kurtosis and outliers can all distort a normal distribution. If a variable has a skewed distribution, it is sometimes possible to transform the variable to normality using a mathematical algorithm so that the outliers in the tail do not bias the summary statistics and P values, or the variable can be analysed using non-parametric tests.

If the sample size is small, say less than 30, outliers in the tail of a skewed distribution can markedly increase or decrease the mean value so that it no longer represents the centre of the data. If the estimate of the centre of the data is inaccurate, then the mean values of two groups will look more alike or more different than the central values actually are and the P value to estimate their difference will be correspondingly reduced or increased. It is important to avoid this type of bias.

Exploratory analyses

The file **surgery.sav** contains data from 141 babies who were referred to a paediatric hospital for surgery. The distributions of three continuous variables in the data set that is birth weight, gestational age and length of stay can be examined using the commands shown in Box 2.2.

Box 2.2 SPSS commands to obtain descriptive statistics and plots

SPSS Commands

```
surgery – SPSS Data Editor
        Analyze → Descriptive Statistics → Explore
Explore
        Highlight variables Birth weight, Gestational age, and Length of stay and
          click into Dependent List
Explore
        Click on Statistics
Explore: Statistics
        Click on Outliers
        Click Continue
Explore
        Click on Plots
Explore: Plots
        Boxplots – Factor levels together (default)
        Descriptive – untick Stem and leaf (default), tick Histogram and tick
           Normality plots with tests
        Click Continue
Explore
        Click on Options
Explore: Options
        Missing Values – tick Exclude cases pairwise
        Click Continue
Explore
        Click OK
```

In the Options menu in Box 2.2, *Exclude cases pairwise* is selected. This option provides information about each variable independently of missing values in the other variables and is the option that is used to describe the entire sample. The default setting for Options is *Exclude cases listwise* but this will exclude a case from the data analysis if there is missing data for any one of the variables entered into the *Dependent List*. The option *Exclude cases listwise* for the data set **surgery.sav** would show that there are 126 babies with complete information for all three continuous variables and 15 babies with missing information for one or more of the three variables. The information for these 126 babies would be important for describing the sample if multivariate statistics that only includes babies without missing data are planned. The characteristics of these 126 babies would be used to describe the generalisability of a multivariate model but not the generalisability of the sample.

Explore

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	**Per cent**	***N***	**Per cent**	***N***	**Per cent**
Birth weight	139	98.6%	2	1.4%	141	100.0%
Gestational age	133	94.3%	8	5.7%	141	100.0%
Length of stay	132	93.6%	9	6.4%	141	100.0%

The Case Processing Summary table shows that two babies have missing birth weights, eight babies have missing gestational age and nine babies have missing length of stay data. This information is important if bivariate statistics will be used in which as many cases as possible are included. The Descriptives table shows the summary statistics for each variable. In the table, all statistics are in the same units as the original variables, that is in grams for birth weight, weeks for gestational age and days for length of stay. The exceptions are the variance, which is in squared units, and the skewness and kurtosis values, which are in units that are relative to a normal distribution.

Descriptives

			Statistic	**Std. error**
Birth weight	Mean		2463.99	43.650
	95% confidence interval for mean	Lower bound	2377.68	
		Upper bound	2550.30	
	5% trimmed mean		2452.53	
	Median		2425.00	
	Variance		264 845.7	
	Std. deviation		514.632	
	Minimum		1150	
	Maximum		3900	
	Range		2750	
	Inter-quartile range		755.00	
	Skewness		0.336	0.206
	Kurtosis		−0.323	0.408
Gestational age	Mean		36.564	0.1776
	95% confidence interval for mean	Lower bound	36.213	
		Upper bound	36.915	
	5% trimmed mean		36.659	
	Median		37.000	

Continued

Descriptives (*Continued)*

			Statistic	Std. error
	Variance		4.195	
	Std. deviation		2.0481	
	Minimum		30.0	
	Maximum		41.0	
	Range		11.0	
	Inter-quartile range		2.000	
	Skewness		−0.590	0.210
	Kurtosis		0.862	0.417
Length of stay	Mean		38.05	3.114
	95% confidence	Lower bound	31.89	
	interval for mean	Upper bound	44.21	
	5% trimmed mean		32.79	
	Median		27.00	
	Variance		1280.249	
	Std. deviation		35.781	
	Minimum		0	
	Maximum		244	
	Range		244	
	Inter-quartile range		21.75	
	Skewness		3.212	0.211
	Kurtosis		12.675	0.419

Normal distribution

A normal distribution such as the distribution shown in Figure 2.2 is classically a bell shaped curve, that is bilaterally symmetrical. If a variable is normally distributed, then the mean and the median values will be approximately equal.

If a normal distribution is divided into quartiles, that is four equal parts, the exact position of the cut-off values for the quartiles is at 0.68 standard deviation above and below the mean. Other features of a normal distribution are that the area of one standard deviation on either side of the mean as shown in Figure 2.2 contains 68% of the values in the sample and the area of 1.96 standard deviations on either side of the mean contains 95% of the values. These properties of a normal distribution are critical for understanding and interpreting the output from parametric tests.

If a variable has a skewed distribution, the mean will be a biased estimate of the centre of the data as shown in Figure 2.3. A variable that has a classically skewed distribution is length of stay in hospital because many patients have a short stay and few patients have a very long stay. When a variable has a skewed distribution, it can be difficult to predict where the centre of the data lies or the range in which the majority of data values fall.

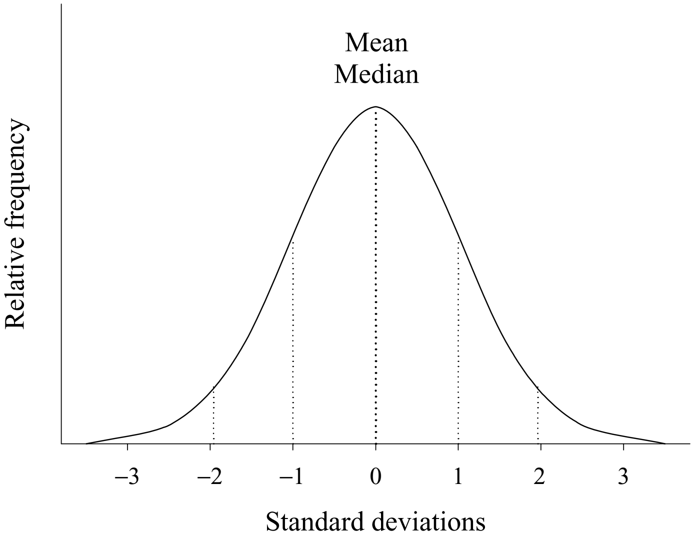


Figure 2.2 Characteristics of a normal distribution.

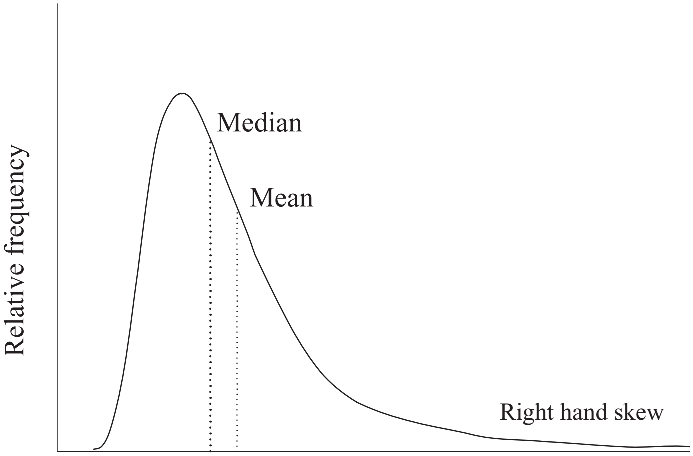


Figure 2.3 Characteristics of a skewed distribution.

For a variable that has a positively skewed distribution with a tail to the right, the mean will usually be larger than the median as shown in Figure 2.3. For a variable with a negatively skewed distribution with a tail to the left, the mean will usually be lower than the median because the distribution will be a mirror image of the curve shown in Figure 2.3. These features of non-normal distributions are helpful in estimating the direction of bias in critical appraisal of studies in which the distribution of the variable has not been taken into account when selecting the statistical tests.

There are several ways of testing whether a continuous variable is normally distributed. Many measurements such as height, weight and blood pressure may be normally distributed in the community but may not be normally distributed if the study has a selected sample or a small sample size. In practice, several checks of normality need to be undertaken to gain a good understanding of the shape of the distribution of each variable in the study sample. It is also important to identify the position of any outliers to gain an understanding of how they may influence the results of any statistical analyses.

The proximity of the mean to the median can indicate possible skewness. A quick informal check of normality is to examine whether the mean and the median values are close to one another. From the Descriptives table, the differences between the median and the mean can be summarised as shown in Table 2.1. The per cent difference is calculated as the difference between the mean and the median as a percentage of the mean.

Table 2.1 Comparisons between mean and median values

Variable	Mean – median	Per cent difference	Interpretation
Birth weight	2464.0 − 2425.0 = 39.0 g	1.5%	Values almost identical, suggesting a normal distribution
Gestational age	36.6 − 37.0 = –0.4 month	1.1%	Values almost identical, suggesting a normal distribution
Length of stay	38.1 − 27.0 = 11.1 days	29.1%	Discordant values, with the mean higher than the median indicating skewness to the right

In Table 2.1, the differences between the mean and median values of birth weight and gestational age are small, suggesting a normal distribution but the large difference between the mean and median values for length of stay suggests that this variable has a non-normal distribution.

An inherent feature of a normal distribution is that 95% of the data values lie between −1.96 standard deviation and +1.96 standard deviations from the mean as shown in Figure 2.2. That is, most data values should lie in the area that is approximately two standard deviations from the mean. Thus, a good approximate check for normality is to double the standard deviation of the variable and then subtract and also add this amount to the mean value. This will give an estimated range in which 95% of the values should lie. The estimated range should be slightly within the actual range of data values, that is the minimum and maximum values. The estimated 95% range for each variable is shown in Table 2.2.

For birth weight and gestational age, the estimated 95% range is within or close to the minimum and maximum values from the Descriptives table. However, for length of stay, the estimated 95% range is not a good approximation

Table 2.2 Calculation of 95% range of variables

Variable	Calculation of range (mean ± 2 SD)	Estimated 95% range	Minimum and maximum values
Birth weight	2464 ± (2 × 514.6)	1434 to 3494	1150 to 3900
Gestational age	36.6 ± (2 × 2.0)	32.6 to 40.6	30.0 to 41.0
Length of stay	38.1 ± (2 × 35.8)	–33.5 to 109.7	0 to 244

of the actual range because the estimated lower value is invalid because it is negative and the estimated upper value is significantly below the maximum value. This is a classical indication of a skewed distribution. If the two estimated values are much less than the actual minimum and maximum values, as in this case, the distribution is usually skewed to the right. If the two estimated values are much higher than the actual minimum and maximum values, the distribution is usually skewed to the left.

A rule of thumb is that a variable with a standard deviation that is larger than one half of the mean value is non-normally distributed, assuming that negative values are impossible[2]. Thus, the mean length of stay of 38.1 days with a standard deviation almost equal to its mean value is an immediate alert to evidence of non-normality.

Skewness and kurtosis

Further information about the distribution of the variables can be obtained from the skewness and kurtosis statistics in the Descriptives table. In SPSS, a perfectly normal distribution has skewness and kurtosis values equal to zero. Skewness values that are positive indicate a tail to the right and skewness values that are negative indicate a tail to the left. Values between −1 and +1 indicate an approximate bell shaped curve and values from −1 to −3 or from +1 to +3 indicate that the distribution is tending away from a bell shape. Any values above +3 or below −3 are a good indication that the variable is not normally distributed.

The Descriptives table shows that the skewness values for birth weight and gestational age are between −1 and 1 suggesting that the distributions of these variables are within the limits of a normal distribution. However, the high skewness value of 3.212 for length of stay confirms a non-normal distribution with a tail to the right.

A kurtosis value above 1 indicates that the distribution tends to be pointed and a value below 1 indicates that the distribution tends to be flat. As for skewness, a kurtosis value between −1 and +1 indicates normality and a value between −1 and −3 or between +1 and +3 indicates a tendency away from normality. Values below −3 or above +3 indicate certain non-normality. For birth weight and gestational age, the kurtosis values are small and are not a cause for concern. However, for length of stay the kurtosis value is 12.675, which indicates that the distribution is peaked in a way that is not consistent with a bell shaped distribution.

Further tests of normality are to divide skewness and kurtosis values by their standard errors as shown in Table 2.3. In practice, dividing a value by its standard error produces a critical value that can be used to judge probability. A critical value that is outside the range of −1.96 to +1.96 indicates that a variable is not normally distributed. The critical values in Table 2.3 confirm that birth weight has a normal distribution with critical values for both skewness and kurtosis below 1.96 and gestational age is deviating from a normal distribution with values outside the critical range of ±1.96. Length of stay is certainly not normally distributed with large critical values of 15.22 and 30.25.

Table 2.3 Using skewness and kurtosis statistics to test for a normal distribution

	Skewness (SE)	Critical value (skewness/SE)	Kurtosis (SE)	Critical value (kurtosis/SE)
Birth weight	0.336 (0.206)	1.63	−0.323 (0.408)	−0.79
Gestational age	−0.590 (0.210)	−2.81	0.862 (0.417)	2.07
Length of stay	3.212 (0.211)	15.22	12.675 (0.419)	30.25

Extreme values and outliers

By requesting outliers in *Analyze → Descriptive Statistics → Explore*, the five largest and five smallest values of each variable and the case numbers or data base rows are shown in the Extreme Values table. Outliers and extreme values that cause skewness must be identified. However, the values printed in the Extreme Values table are the minimum and maximum values in the data set and these may not be influential outliers.

Extreme Values

			Case number	Value
Birth weight	Highest	1	5	3900
		2	54	3545
		3	16	3500
		4	50	3500
		5	141	3500
	Lowest	1	4	1150
		2	103	1500
		3	120	1620
		4	98	1680
		5	38	1710

Continued

			Case number	Value
Gestational age	Highest	1	85	41.0
		2	11	40.0
		3	26	40.0
		4	50	40.0
		5	52	40.0[a]
	Lowest	1	2	30.0
		2	79	31.0
		3	38	31.0
		4	4	31.0
		5	117	31.5
Length of stay	Highest	1	121	244
		2	120	211
		3	110	153
		4	129	138
		5	116	131
	Lowest	1	32	0
		2	33	1
		3	12	9
		4	22	11
		5	16	11

[a] Only a partial list of cases with the value 40.0 are shown in the table of upper extremes.

Statistical tests of normality

By requesting normality plots in *Analyze* → *Descriptive Statistics* → *Explore*, the following tests of normality are obtained:

Tests of Normality

	Kolmogorov–Smirnov[a]			Shapiro–Wilk		
	Statistic	*df*	Sig.	Statistic	*df*	Sig.
Birth weight	0.067	139	0.200*	0.981	139	0.056
Gestational age	0.151	133	0.000	0.951	133	0.000
Length of stay	0.241	132	0.000	0.643	132	0.000

* This is a lower bound of the true significance.

[a] Lilliefors significance correction.

The Tests of Normality table provides the results of two tests: a Kolmogorov–Smirnov statistic with a Lilliefors significance correction and a Shapiro–Wilk statistic. A limitation of the Kolmogorov–Smirnov test of normality without the Lilliefors correction is that it is very conservative and is sensitive to extreme values that cause tails in the distribution. The Lilliefors significance correction renders this test a little less conservative. The Shapiro–Wilk test has more statistical power to determine a non-normal distribution than the Kolmogorov–Smirnov test[3]. The Shapiro–Wilk test is based on the correlation between the data and the corresponding normal scores and will have a value of 1.0 for perfect normality.

A distribution that passes these tests of normality provides extreme confidence that parametric tests can be used. However, variables that do not pass these tests may not be so non-normally distributed that parametric tests cannot be used, especially if the sample size is large. This is not to say that the results of these tests can be ignored but rather that a considered decision using the results of all the available tests of normality needs to be made.

For both the Shapiro–Wilk and Kolmogorov–Smirnov tests, a *P* value less than 0.05 indicates that the distribution is significantly different from normal. The *P* values are shown in the column labelled Sig. in the Tests of Normality table. Birth weight marginally fails the Shapiro–Wilk test but the *P* values for gestational age and length of stay show that they have potentially non-normal distributions. The Kolmogorov–Smirnov test shows that the distribution of birth weight is not significantly different from a normal distribution with a *P* value greater than 0.2. However, the Kolmogorov–Smirnov test indicates that the distributions of both gestational age and length of stay are significantly different from a normal distribution at $P < 0.0001$.

These tests of normality do not provide any information about why a variable is not normally distributed and therefore, it is always important to obtain skewness and kurtosis values using *Analyze → Descriptive Statistics → Explore* and to request plots in order to identify any reasons for non-normality.

Normality plots

Finally, from the commands in Box 2.2, descriptive and normality plots were requested for each variable. All of the plots should be inspected because each plot gives very different information.

The histograms show the frequency of measurements and the shape of the data and therefore provide a visual judgement of whether the distribution approximates to a bell shape. Histograms also show whether there are any gaps in the data, whether there are any outlying values and how far any outlying values are from the remainder of the data.

The normal Q–Q plot shows each data value plotted against the value that would be expected if the data came from a normal distribution. The values in the plot are the quantiles of the variable distribution plotted against the quantiles that would be expected if the distribution was normal. If the variable was normally distributed, the points would fall directly on the straight line. Any deviations from the straight line indicate some degree of non-normality.

The detrended normal Q–Q plots show the deviations of the points from the straight line of the normal Q–Q plot. If the distribution is normal, the points will cluster randomly around the horizontal line at zero with an equal spread of points above and below the line. If the distribution is non-normal, the points will be in a pattern such as J or an inverted U distribution and the horizontal line may not be in the centre of the data.

The box plot shows the median as the black horizontal line inside the box and the inter-quartile range as the length of the box. The inter-quartile range indicates the 25th to 75th percentiles, that is the range in which the central 25% to 75% of the data points lie. The whiskers are the lines extending from the top and bottom of the box. The whiskers represent the minimum and maximum values when they are within 1.5 times above or below the inter-quartile range. If values are outside this range, they are plotted as outlying or extreme values.

Any outlying values that are between 1.5 and 3 box lengths from the upper or lower edge of the box are shown as open circles, and are identified with the corresponding number of the data base row. Extreme values that are more than three box lengths from the upper or lower edge of the box are shown as asterisks. Extreme and/or outlying values should be checked to see whether they are univariate outliers (Chapter 3). If there are several extreme values at either end of the range of the data or the median is not in the centre of the box, the variable will not be normally distributed. If the median is closer to the bottom end of the box than to the top, the data are positively skewed. If the median is closer to the top end of the box, the data are negatively skewed.

In Figure 2.4 the histogram for birth weight shows that this distribution is not strictly bell shaped but the normal Q–Q plot follows an approximately normal distribution apart from the tails, and the box plot is symmetrical with no outlying or extreme values. These features indicate that the mean value will be an accurate estimate of the centre of the data and that the standard deviation will accurately describe the spread.

In Figure 2.5 the histogram for gestational age shows that this distribution has a small tail to the left and only deviates from normal at the lower end of the normal Q–Q plot. The box plot for this variable appears to be symmetrical but has a few outlying values and one extreme value at the lower end of the data values.

In contrast, in Figure 2.6 the histogram for length of stay has a marked tail to the right so that the distribution deviates markedly from a straight line on the normal Q–Q plot. On the detrended normal Q–Q plot, the pattern is similar to a U shape. The box plot shows many outlying values and multiple extreme values at the upper end of the distribution. Some of the outlying and extreme values overlap each other so that it is difficult to identify the cases. By double clicking on the box plot, the plot will be enlarged in the *Chart Editor* and the case numbers can be seen more clearly. By clicking on the case numbers, the display option can be altered so that the outliers and/or extreme values can be identified by their ID or case number.

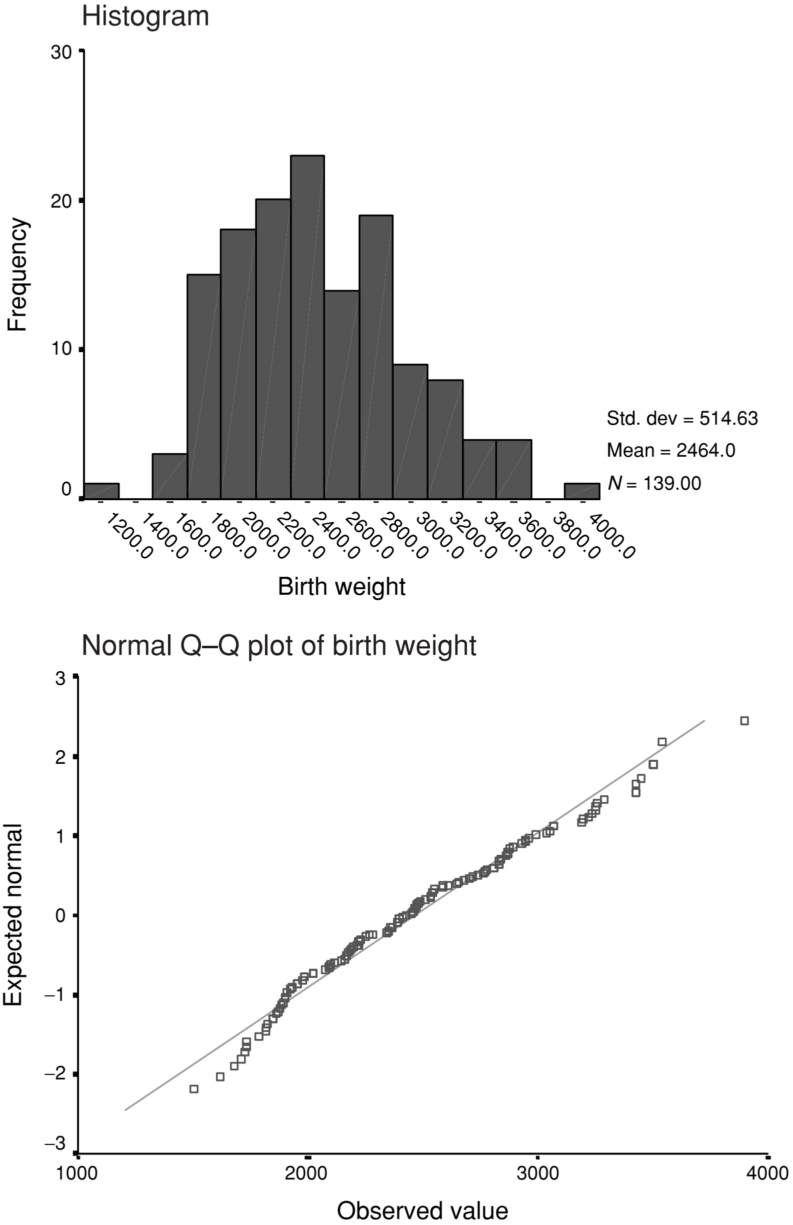
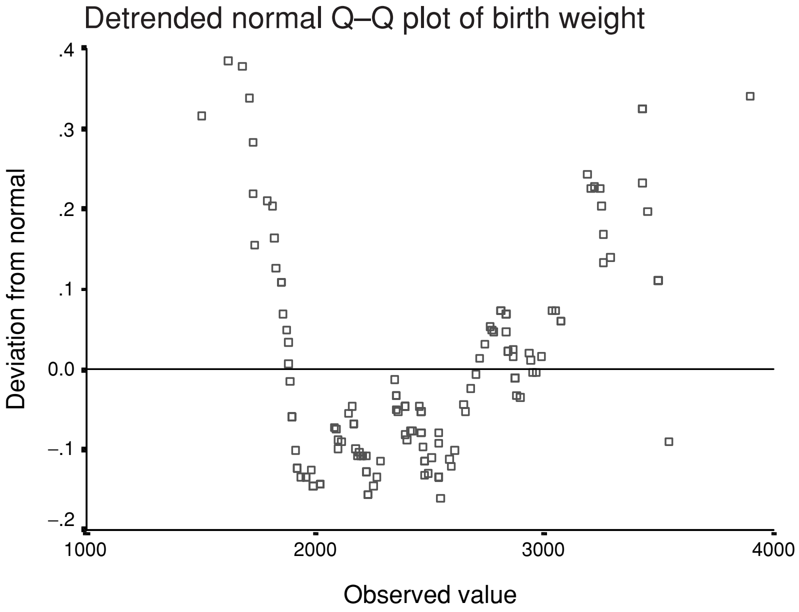


Figure 2.4 Plots of birth weight.



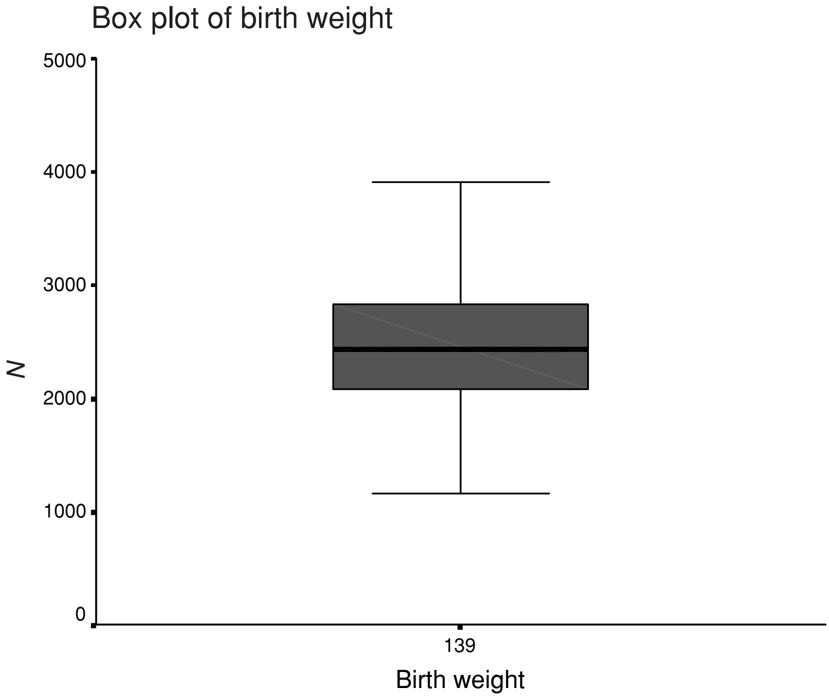
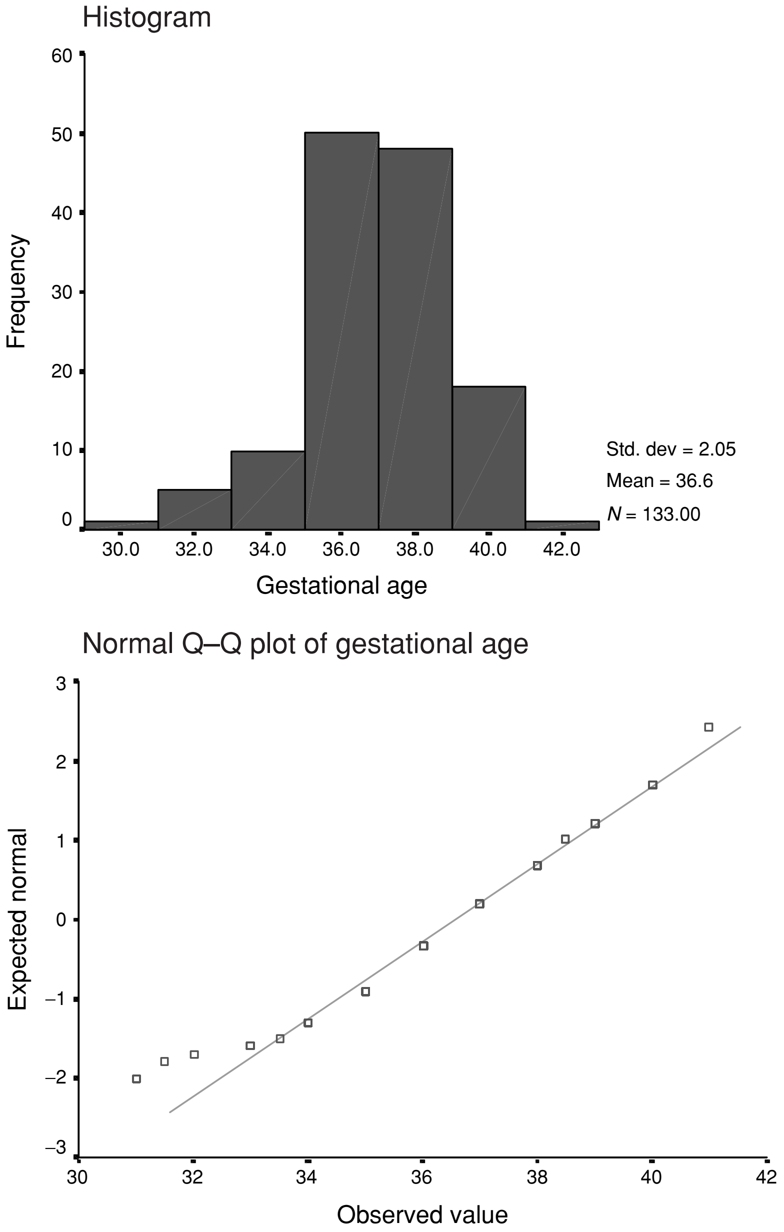


Figure 2.4 *Continued*



Histogram

Normal Q–Q plot of gestational age

Figure 2.5 Plots of gestational age.

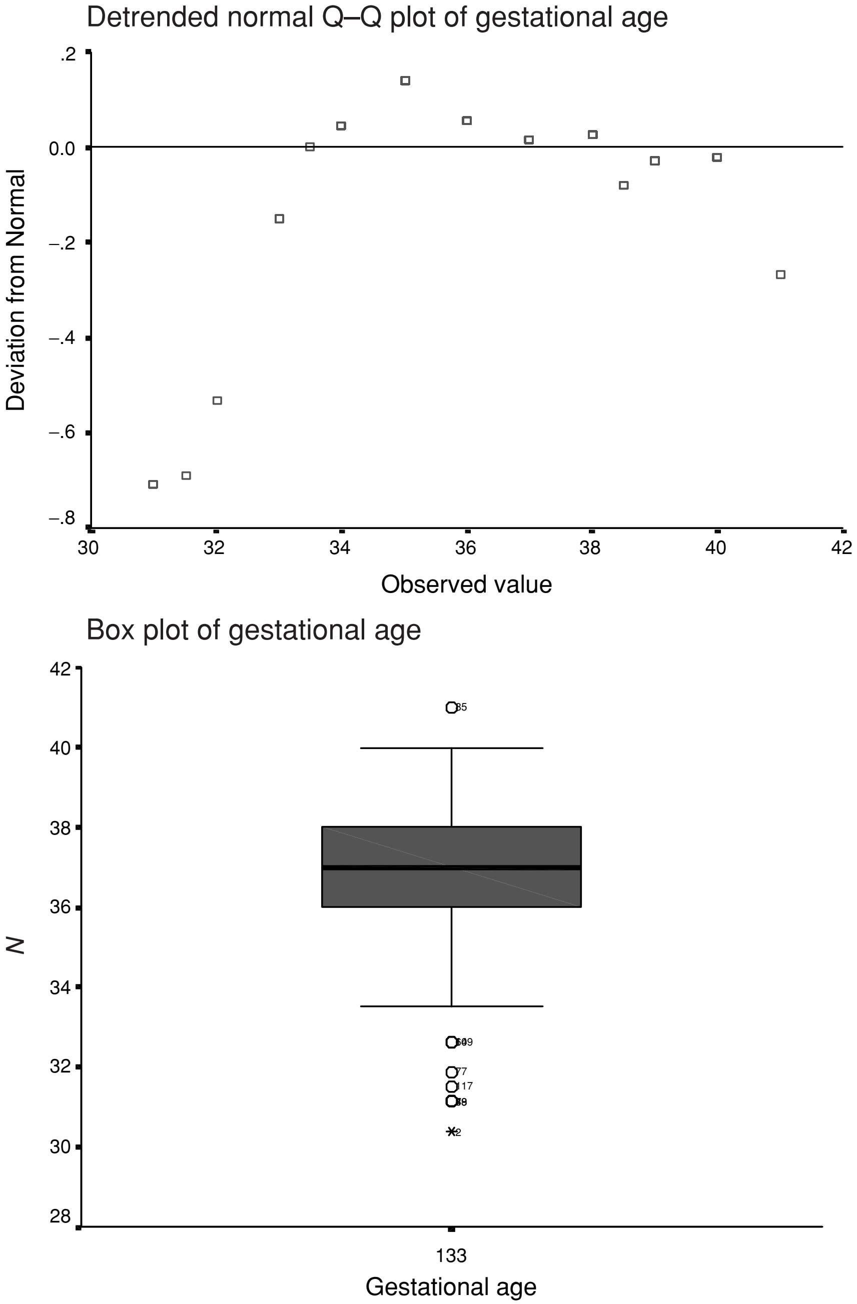


Figure 2.5 *Continued*

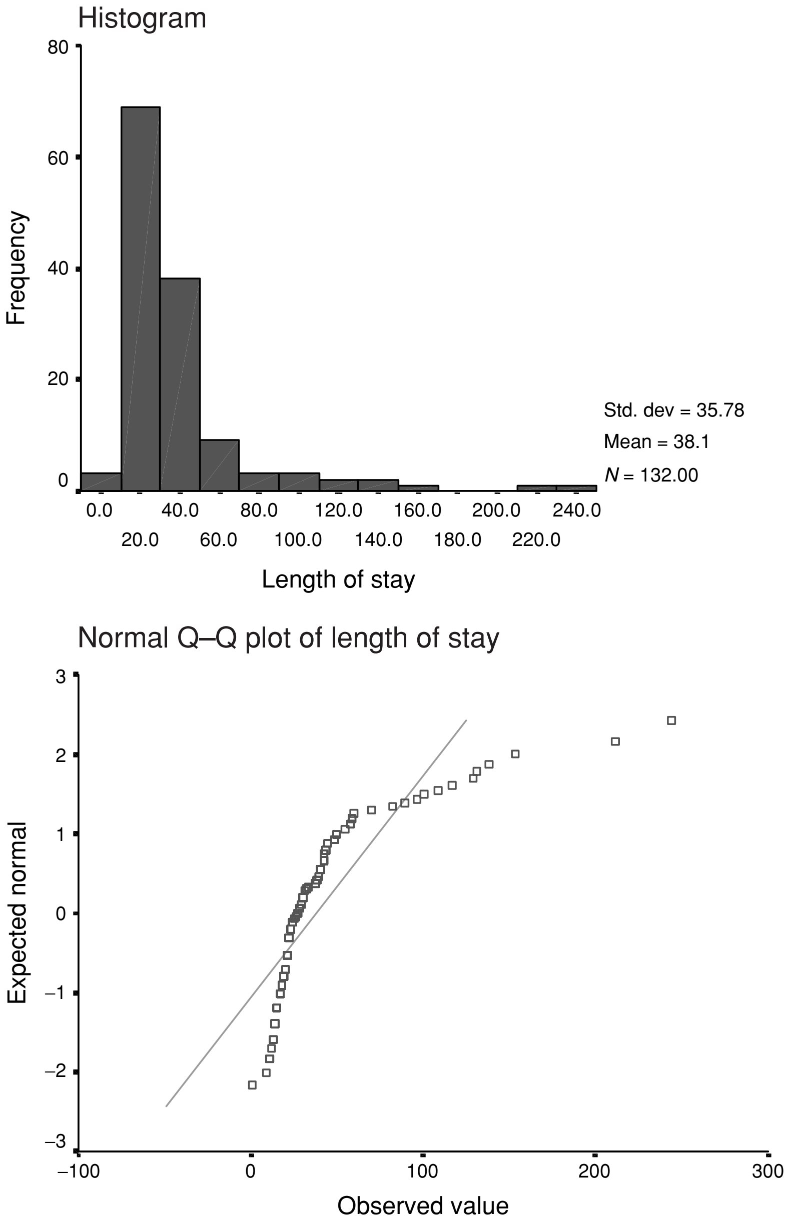
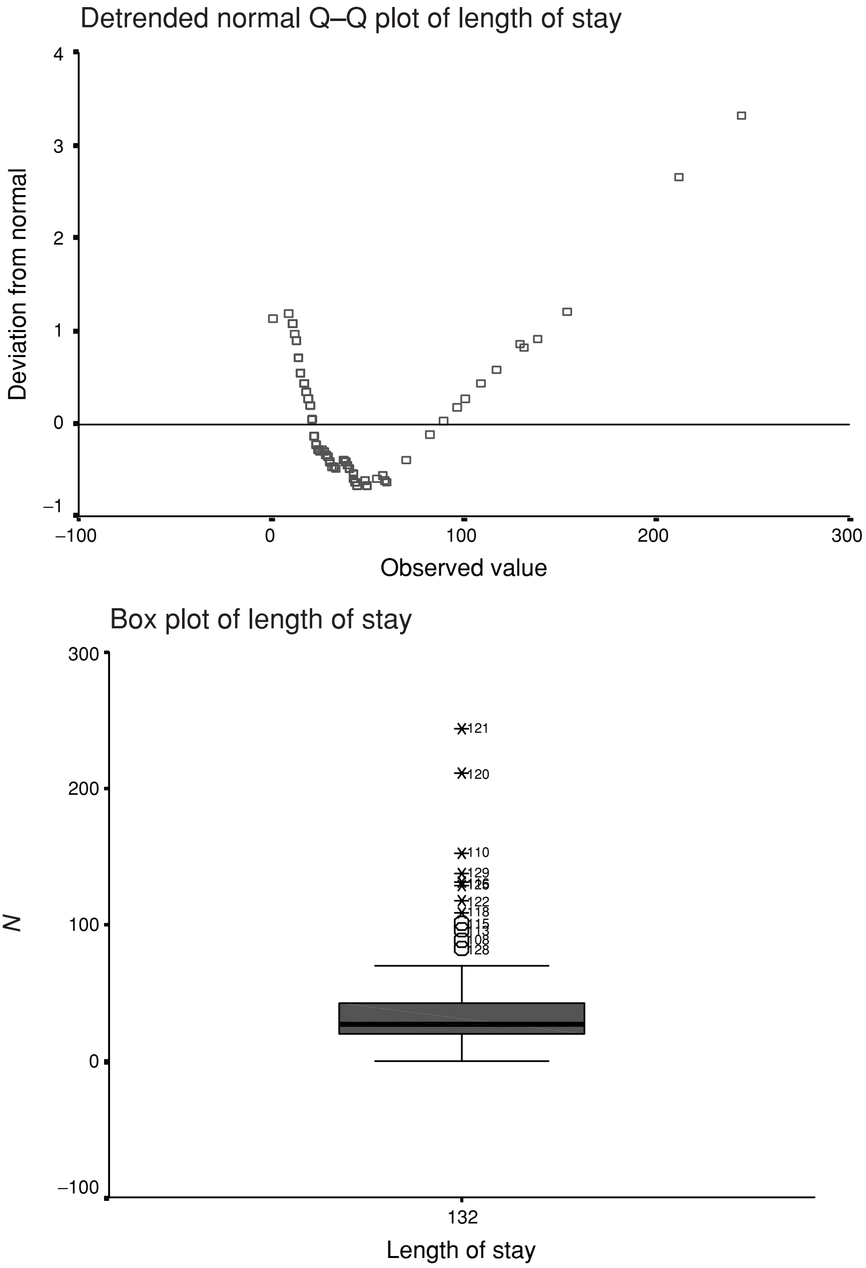


Figure 2.6 Plots of length of stay.


Detrended normal Q–Q plot of length of stay

Box plot of length of stay

Figure 2.6 *Continued*

Kolmogorov–Smirnov test

In addition to the above tests of normality, a Kolmogorov–Smirnov test can be obtained as shown in Box 2.3.

Box 2.3 SPSS commands to conducting a one sample of normality

SPSS Commands

surgery – SPSS Data Editor
Analyze → Non parametric Tests → 1-Sample K-S
One-Sample Kolmogorov-Smirnov Test
Highlight Birth weight, Gestational age, Length of stay and click into Test Variable List
Test Distribution - tick Normal (default)
Click on Options
One-sample K-S: Options
Missing Values – tick Exclude cases test-by-test (default)
Click Continue
One-Sample Kolmogorov-Smirnov Test
Click OK

NPar Tests

One-Sample Kolmogorov–Smirnov Test

		Birth weight	Gestational age	Length of stay
N		139	133	132
Normal parameters[a,b]	Mean	2463.99	36.564	38.05
	Std. deviation	514.632	2.0481	35.781
Most extreme	Absolute	0.067	0.151	0.241
Differences	Positive	0.067	0.105	0.241
	Negative	−0.043	−0.151	−0.202
Kolmogorov–Smirnov *Z*		0.792	1.741	2.771
Asymp. sig. (two-tailed)		0.557	0.005	0.000

[a] Test distribution is normal.
[b] Calculated from data.

The *P* values for the test of normality in the One-Sample Kolmogorov–Smirnov Test table are different from Kolmogorov–Smirnov *P* values obtained in *Analyze → Descriptive Statistics → Explore* because the one-sample test shown here is without the Lilliefors correction. Without the correction applied this test, which is based on slightly different assumptions about the mean and the variance of the normal distribution being tested for fit, is extremely conservative. Once again, the *P* values suggest that birth weight is normally distributed but gestational age and length of stay do not pass this test of normality with *P* values less than 0.05.

Table 2.4 Summary of whether descriptive statistics and plots indicate a normal distribution

	Mean–median	Mean ± 2 SD	Skewness and kurtosis	Critical values	K-S test	Plots	Overall decision
Birth weight	Probably	Yes	Yes	Yes	Yes	Probably	Yes
Gestational age	Yes	Yes	Yes	No	No	Probably	Yes
Length of stay	No	No	No	No	No	No	No

Deciding whether a variable is normally distributed

The information from the descriptive statistics and normality plots can be summarised as shown in Table 2.4. In the table, Yes indicates that the distribution is within normal range and No indicates that the distribution is outside the normal range.

Clearly, the results of tests of normality are not always in agreement. By considering all of the information together, a decision can be made about whether the distribution of each variable is normal enough to justify using parametric tests or whether the deviation from normal is so marked that non-parametric or categorical tests need to be used. These decisions, which sometimes involve subjective judgements, should be based on all processes of checking for normality.

Table 2.4 shows that parametric tests are appropriate for analysing birth weight because this variable is normally distributed. The variable gestational age is approximately normally distributed with some indications of a small deviation. However the mean value is a good estimate of the centre of the data. Parametric tests are robust to some deviations from normality if the sample size is large, say greater than 100 as is this sample. If the sample size had been small, say less than 30, then this variable would have to be perfectly normally distributed rather than approximately normally distributed before parametric tests could be used.

Length of stay is clearly not normally distributed and therefore this variable needs to be either transformed to normality to use parametric tests, analysed using non-parametric tests or transformed to a categorical variable. There are a number of factors to consider in deciding whether a variable should be transformed. Parametric tests generally provide more statistical power than non-parametric tests but if a parametric test does not have a non-parametric equivalent then transformation is essential. However, transformation can increase difficulties in interpreting the results because few people think naturally in transformed units. For example, if length of stay is transformed by calculating its square root, the results of parametric tests will be presented in units of the square root of length of stay and will be more difficult to interpret and to compare with results from other studies.

Transforming skewed distributions

Various mathematical formulae can be used to transform a skewed distribution to normality. When a distribution has a marked tail to the right hand side, a logarithmic transformation of scores is often effective[4]. The advantage of logarithmic transformations is that they give interpretable results after being back-transformed into original units[5]. Other common transformations include square roots and reciprocals[6]. When data are transformed and differences in transformed mean values between two or more groups are compared, the summary statistics will not apply to the means of the original data but will apply to the medians of the original data[6].

Length of stay can be transformed to logarithmic values using the commands shown in Box 2.4. The transformation LG10 can be clicked in from the Functions box and the variable can be clicked in from the variable list. Either base e or base 10 logarithms can be used but base 10 logarithms are a little more intuitive in that 0 = 1 (10^0), 1 = 10 (10^1), 2 = 100 (10^2), etc. and are therefore a little easier to interpret and communicate. When using logarithms, any values that are zero will naturally be declared as invalid and registered as missing values in the transformed variable.

Box 2.4 SPSS commands for computing a new variable

SPSS Commands

surgery - SPSS Data Editor

Transform → Compute

Compute Variable

Target Variable = LOS2

Scroll down Functions and highlight LG10 (numexpr) and click the arrow next to Functions

Click Length of stay from the Variable list to obtain Numeric Expression = LG10 (lengthst)

Click OK

On completion of the logarithmic transformation, an error message will appear in the output viewer of SPSS specifying any case numbers that have been set to system missing. In this data set, case 32 has a value of zero for length of stay and has been transformed to a system missing value for logarithmic length of stay. If there are only a few cases that cannot be log transformed, the number of system missing values may not be important. However if many cases have zero or negative values, a constant can be added to each value to ensure that the logarithmic transformation can be undertaken[7]. For example, if the minimum value is –2.2, then a constant of 3 can be added to all values. This value can be subtracted again when the summary statistics are transformed back to original units.

Whenever a new variable is created, it must be labelled and its format must be adjusted. The log-transformed length of stay can be re-assigned in Variable View by adding a label 'Log length of stay' to ensure that the output is self-documented. In addition, the number of decimal places can be adjusted to an appropriate number, in this case three. Once a newly transformed variable is obtained, its distribution must be checked again using the *Analyze → Descriptive Statistics → Explore* commands shown in Box 2.2, which will provide the following output.

Explore

Case Processing Summary

	Cases					
	Valid		**Missing**		**Total**	
	N	Per cent	*N*	Per cent	*N*	Per cent
Log length of stay	131	92.9%	10	7.1%	141	100.0%

The Case Processing Summary table shows that there are now 131 valid cases for log-transformed length of stay compared with 132 valid cases for length of stay because case 32, which had a zero value, could not be transformed and has been assigned a system missing value.

Descriptives

			Statistic	**Std. error**
Log length of stay	Mean		1.4725	0.02623
	95% confidence interval for mean	Lower bound	1.4206	
		Upper bound	1.5244	
	5% trimmed mean		1.4644	
	Median		1.4314	
	Variance		0.090	
	Std. deviation		0.30018	
	Minimum		0.00	
	Maximum		2.39	
	Range		2.39	
	Inter-quartile range		0.3010	
	Skewness		−0.110	0.212
	Kurtosis		4.474	0.420

The Descriptives table shows that mean log length of stay is 1.4725 and the median value is 1.4314. The two values are only 0.0411 units apart, which suggests that the distribution is now much closer to being normally distributed. Also, the skewness value is now closer to zero, indicating no significant skewness. The kurtosis value of 4.474 indicates that the distribution remains peaked, although not as markedly as before. The values for two standard deviations below and above the mean value, that is $1.4725 \pm (2 \times 0.3)$ or 0.87 and 2.07 respectively, are much closer to the minimum and maximum values of 0 and 2.39 for the variable.

Following transformation there is no need to request information of extreme values because the same data points are still the extreme points.

Dividing skewness by its standard error, that is $-0.110/0.212$, gives the critical value of -0.52, indicating a normal distribution. However, dividing the kurtosis by its standard error, that is 4.474/0.42, gives the critical value of 10.65, confirming that the distribution remains too peaked to conform to normality. In practice, peakness is not as important as skewness for deciding when to use parametric tests because deviations in kurtosis do not bias mean values.

Tests of Normality

	Kolmogorov–Smirnov[a]			**Shapiro-Wilk**		
	Statistic	***df***	**Sig.**	**Statistic**	***df***	**Sig.**
Log length of stay	0.097	131	0.004	0.916	131	0.000

[a] Lilliefors Significance Correction.

In the Tests of Normality table, the results of the Kolmogorov–Smirnov and Shapiro–Wilk tests indicate that the distribution remains significantly different from a normal distribution at $P = 0.004$ and $P < 0.0001$ respectively.

The histogram for the log-transformed variable shown in Figure 2.7 conforms to a bell shape distribution better than the original variable except for some outlying values in both tails and a gap in the data on the left. Such gaps are a common feature of data distributions when the sample size is small but they need to be investigated when the sample size is large as in this case. The lowest extreme value for log length of stay is a univariate outlier. Although log length of stay is not perfectly normally distributed, it will provide less biased P values than the original variable if parametric tests are used.

Care must be taken when transforming summary statistics in log units back into their original units[5]. In general, it is best to carry out all statistical tests using the transformed scale and only transform summary statistics back into original units in the final presentation of the results. Thus, the interpretation of the statistics should be undertaken using summary statistics of the transformed variable. When a logarithmic mean is anti-logged it is called a geometric mean. The standard deviation (spread) cannot be back transformed to have the usual interpretation although the 95% confidence interval can be back transformed and will have the usual interpretation.

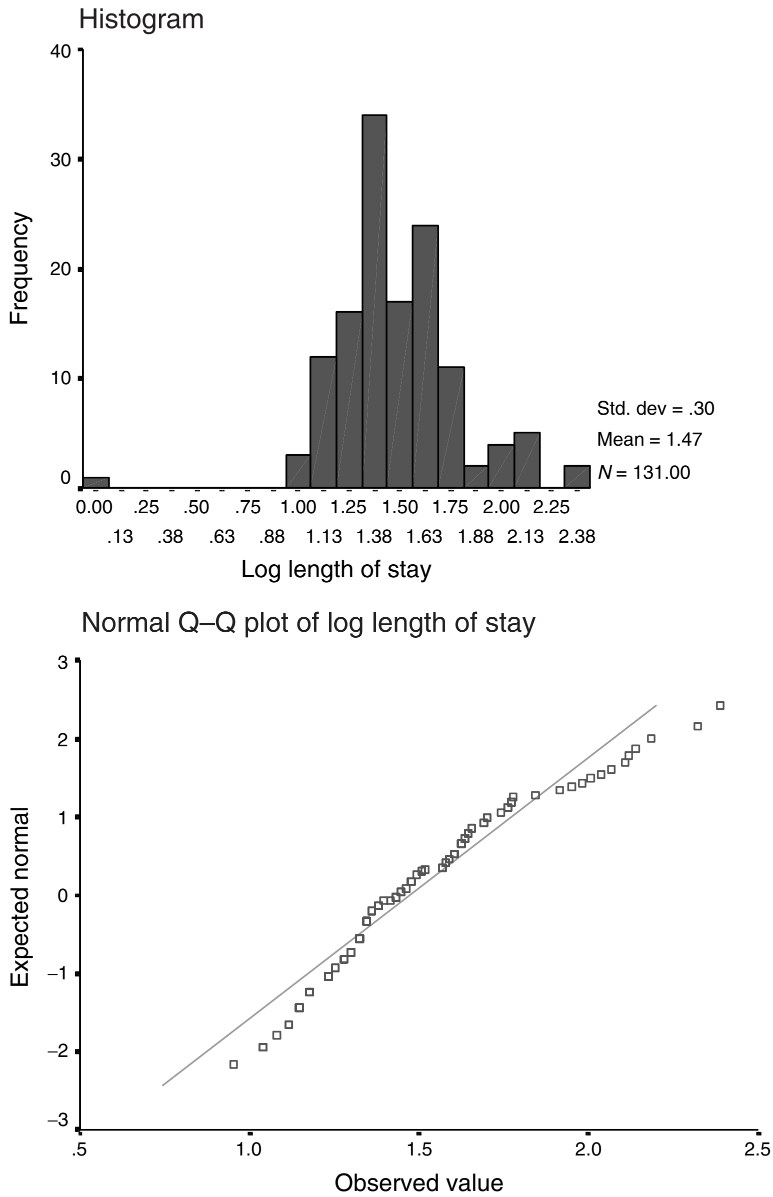


Figure 2.7 Plots of log length of stay.

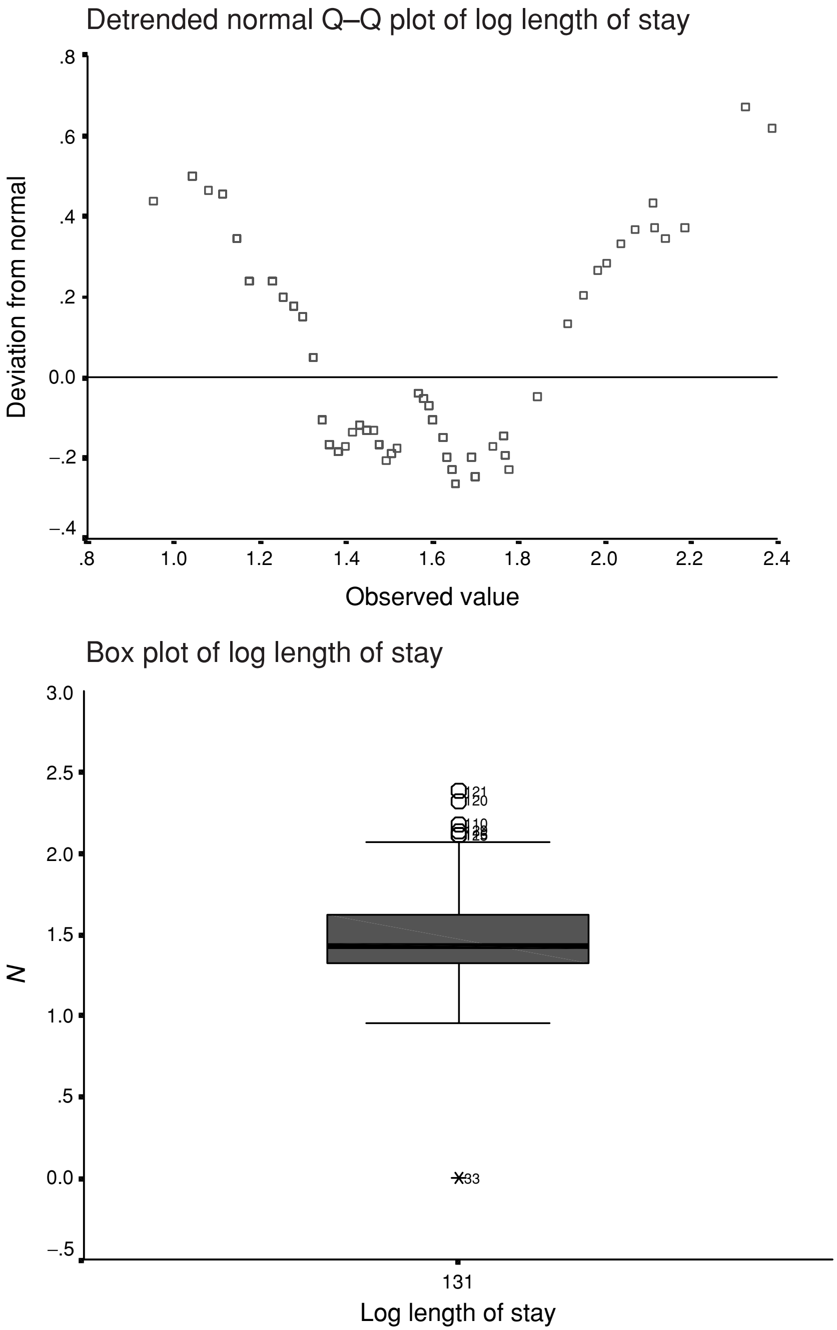


Figure 2.7 *Continued*

Summarising descriptive statistics

In all research studies, it is important to report details of the characteristics of the study sample or study groups to describe the generalisability of the results. For this, statistics that describe the centre of the data and its spread are appropriate. Therefore, for variables that are normally distributed, the mean and the standard deviation are reported. For variables that are non-normally distributed, the median and the inter-quartile range are reported.

Statistics of normally distributed variables that describe precision, that is the standard error and 95% confidence interval, are more useful for comparing groups or making inferences about differences between groups. Table 2.5 shows how to present the characteristics of the babies in the **surgery.sav** data set. In presenting descriptive statistics, no more than one decimal point greater than in the units of the original measurement should be used[8].

Table 2.5 Baseline characteristics of the study sample

Characteristic	*N*	Distribution in sample Mean (SD) or median (IQ range)
Birth weight	139	2464.0 g (SD 514.6)
Gestational age	133	36.6 weeks (SD 2.0)
Length of stay	132	27.0 days (IQ range 21.8 days)

Testing for normality in published results

When critically appraising journal articles, it may be necessary to transform a measure of spread to a measure of precision, or vice versa, for comparing with results from other studies. Computing a standard deviation from a standard error, or vice versa, is simple because the formula is

$$\text{Standard error (SE)} = \text{Standard deviation (SD)}/\sqrt{n}$$

where n is the sample size.

Also, by adding and subtracting two standard deviations from the mean, it is possible to roughly estimate whether the distribution of the data conforms to a bell shaped distribution. For example, Table 2.6 shows summary statistics of lung function shown as the mean and standard deviation in a sample of children with severe asthma. In this table, FEV_1 is forced expiratory volume in one second and it is rare that this value would be below 30%, even in a child with severe lung disease.

Table 2.6 Mean lung function values of two study groups

%predicted normal value	Active group	Control group	*P* value
FEV_1 (mean ± SD)	37.5 ± 16.0	36.0 ± 15.0	0.80

In the active group, the lower value of the 95% range of per cent predicted FEV_1 is 37.5% – (2 × 16.0)%, which is 5.5%. Similarly the lower value of

95% range for the control group is 6.0%. Both of these values for predicted FEV$_1$ are implausible and are a clear indication that the data are skewed, that the standard deviation is not an appropriate statistic to describe the spread of the data and that parametric tests cannot be used to compare the groups.

If the lower estimate of the 95% range is too low, as in Table 2.6, the mean will be an overestimate of the median value. If the lower estimate is too high, the mean value will be an underestimate of the median value. In Table 2.6, the variables are significantly skewed with a tail to the right hand side. In this case, the median and inter-quartile range would provide more accurate estimates of the centre, of the differences between the groups and spread of the data and non-parametric tests would be needed to compare the groups.

Notes for critical appraisal

Questions to ask when assessing descriptive statistics published in the literature are shown in Box 2.5.

Box 2.5 Questions for critical appraisal

The following questions should be asked when appraising published results:

- Have several tests of normality been considered and reported?
- Are appropriate statistics used to describe the centre and spread of the data?
- Do the values of the mean ±2 SD represent a reasonable 95% range?
- If a distribution is skewed, has the mean of either group been underestimated or overestimated?
- If the data are skewed, have the median and inter-quartile range been reported?

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CHAPTER 3
Continuous variables: comparing two independent samples

Do not put faith in what statistics say until you have carefully considered what they do not say.
WILLIAM W. WATT

Objectives

The objectives of this chapter are to explain how to:

- conduct an independent two-sample parametric or non-parametric test
- assess for homogeneity of variances
- interpret effect sizes and 95% confidence intervals
- report the results in a table or a graph
- critically appraise the analysis of data from two independent groups in the literature

Comparing the means of two independent samples

A two-sample *t*-test is a parametric test used to estimate whether the mean value of a normally distributed outcome variable is significantly different between two groups of participants. This test is also known as a Student's *t*-test or an independent samples *t*-test. Two-sample *t*-tests are classically used when the outcome is a continuous variable and when the explanatory variable is binary. For example, this test would be used to assess whether mean height is significantly different between a group of males and a group of females.

A two-sample *t*-test is used to assess whether two mean values are similar enough to have come from the same population or whether their difference is large enough for the two groups to have come from different populations. Rejecting the null hypothesis of a two-sample *t*-test indicates that the difference in the means of the two groups is large and is not due to either chance or sampling variation.

The assumptions that must be met to use a two-sample *t*-test are shown in Box 3.1.

Box 3.1 Assumptions for using a two-sample *t*-test

The assumptions that must be satisfied to conduct a two-sample *t*-test are:

- the groups must be independent, that is each participant must be in one group only
- the measurements must be independent, that is a participant's measurement can be included in their group once only
- the outcome variable must be on a continuous scale
- the outcome variable must be normally distributed in each group

The first two assumptions in Box 3.1 are determined by the study design. To conduct a two-sample *t*-test, each participant must be on a separate row of the spreadsheet and each participant must be included in the spreadsheet once only. In addition, one of the variables must indicate the group to which the participant belongs.

The fourth assumption that the outcome variable must be normally distributed in each group must also be met. If the outcome variable is not normally distributed in each group, a non-parametric test or a transformation of the outcome variable will be needed. However, two-sample *t*-tests are fairly robust to some degree of non-normality if the sample size is large and if there are no influential outliers. The definition of a 'large' sample size varies but there is common consensus that *t*-tests can be used when the sample size of each group contains at least 30 to 50 participants. If the sample size is less than 30, if outliers significantly influence one of the distributions or if the distribution is non-normal, then a two-sample *t*-test should not be used.

One- and two-tailed tests

When a hypothesis is tested, it is possible to conduct a one-tailed (sided) or a two-tailed (sided) test. A one-tailed test is used to test an effect in one direction only (i.e. $\text{mean}_1 > \text{mean}_2$) whereas a two-tailed test is used to decide whether one mean value is smaller or larger than another mean value (i.e. $\text{mean}_1 \neq \text{mean}_2$). In the majority of studies, it is important to always use a two-tailed test. If a one-tailed test is used, the direction should be specified in the study design prior to data collection. As shown in Figure 3.1, a two-tailed test halves the level of significance (i.e. 0.05) in each tail of the distribution.

Assuming that the null hypothesis of no difference between population means is true and pairs of samples were repeatedly compared to each other, in 95% of the cases the observed *t* values would fall within the critical *t* value range and differences would be due to sampling error. Observed *t* values that fall outside this critical range, which occurs in 5% of the cases, represent an unlikely *t* value to occur when the null hypothesis is true, therefore the null hypothesis is rejected.

For a two-tailed test, 2.5% of the rejection region is placed in the positive tail of the distribution (i.e. $\text{mean}_1 > \text{mean}_2$) and 2.5% is placed in the negative tail (i.e. $\text{mean}_1 < \text{mean}_2$). When a one-tailed test is used, the 5% rejection region

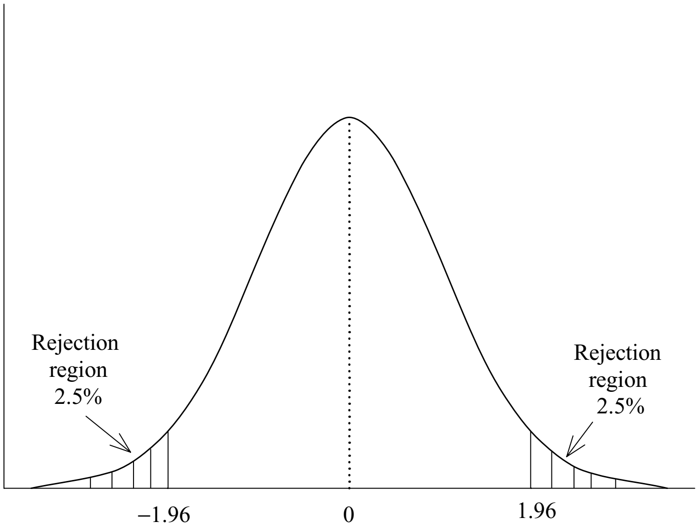

Figure 3.1 Statistical model and rejection regions for a two-tailed *t*-test with $P = 0.05$.

is placed only in one tail of the distribution. For example, if the hypothesis $\text{mean}_1 > \text{mean}_2$ was being tested, the 5% rejection region would be in the positive end of the tail. This means that for one-tailed tests, *P* values on the margins of significance are reduced and that the difference is more likely to be significant. For this reason, one-tailed tests are rarely used in health research.

Homogeneity of variance

In addition to testing for normality, it is also important to inspect whether the variance (the square of the standard deviation) in each group is similar, that is whether there is homogeneity of variances between groups. If the variance is different between the two groups, that is there is heterogeneity of variances, then the degrees of freedom and *t* value associated with a two-sample *t*-test are calculated differently. In this situation, a fractional value for degrees of freedom is used and the *t*-test statistics is calculated using individual group variances. In SPSS, Levene's test for equality of variances is an automatic part of the two-sample *t*-test routine and the information is printed in the SPSS output.

Effect size

Effect size is a term used to describe the size of the difference in mean values between two groups relative to the standard deviation. Effect sizes are important because they can be used to describe the magnitude of the difference between two groups in either experimental or observational study designs. The effect size between two independent groups is calculated as follows:

$$\text{Effect size} = (\text{Mean}_2 - \text{Mean}_1)/\text{SD}$$

where SD denotes the standard deviation.

Effect sizes are measured in units of the standard deviation. The standard deviation around each group's mean value indicates the spread of the measurements in each group and is therefore useful for describing the distance between the two mean values. If the variances of the two groups are homogeneous then the standard deviation of either group can be used in calculating the effect size[1]. If there is an experimental group (i.e. a group in which a treatment is being tested) and a control group, the standard deviation of the control group should be used. If the sample size of the control group is large, the standard deviation will be an unbiased estimate of the population who have not been given the treatment. When the sample size is small or when there is no control group, the pooled standard deviation, which is the average of the standard deviations of the two groups, is used. The pooled standard deviation is the root mean square of the two standard deviations and is calculated as:

$$\text{Pooled standard deviation} = \sqrt{\left[\frac{(\mathrm{SD}_1{}^2 + \mathrm{SD}_2{}^2)}{2}\right]}$$

where SD_1 = standard deviation of group 1 and SD_2 = standard deviation of group 2.

An effect size of 0.2 is considered small, 0.5 is considered medium and 0.8 is considered large[2]. Effect size is generally interpreted assuming that the two groups have a normal distribution and can be considered as the average percentile ranking of the experimental group relative to the control group. Therefore, an effect size of 1 indicates that the mean of the experimental group is at the 84th percentile of the control group[1].

Figure 3.2 shows the distribution of a variable in two groups that have mean values that are one standard deviation apart, that is an effect size of 1 SD.

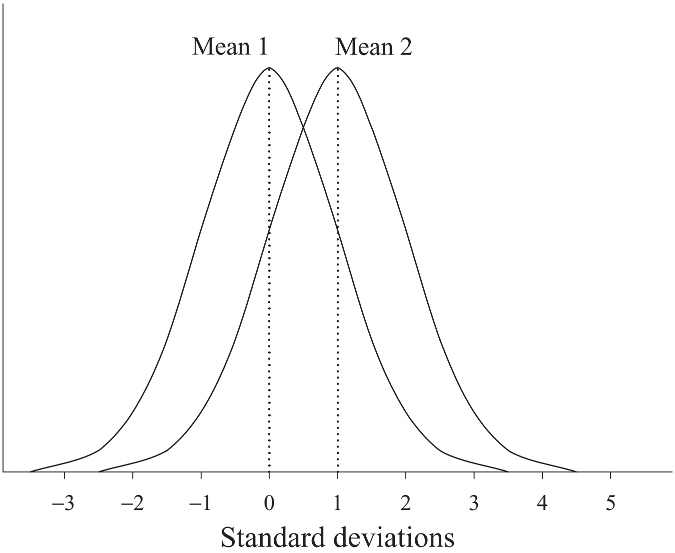

Figure 3.2 Mean values of two groups that are one standard deviation apart.

Study design

Two-sample t-tests can be used to analyse data from any type of study design where the explanatory variable falls into two groups, e.g. males and females, cases and controls, and intervention and non-intervention groups. For a two-sample t-test, there must be no relation or dependence between the participants in each of the two groups. Therefore, two-sample t-tests cannot be used to analyse scores from follow-up studies where data from a participant are obtained on repeated occasions for the same measure or for matched case-control studies in which participants are treated as pairs in the analyses. In these types of studies, a paired t-test should be used.

It is important to interpret significant P values in the context of the size of the difference between the groups and the sample size. The size of the study sample is an important determinant of whether a difference in means between two groups is statistically significant. Ideally, studies should be designed and conducted with a sample size that is sufficient for a clinically important difference between two groups to become statistically significant.

If a small effect size and/or a lower level of significance is used, then a large sample size will be needed to detect the effect with sufficient power[2]. When designing a study, a power analysis should be conducted to calculate the sample size that is needed to detect a pre-determined effect size with sufficient statistical power. If the sample size is too small, then type II errors may occur, that is a clinically important difference between groups will not be statistically significant. The influence of sample size can make the results of statistical tests difficult to interpret. In addition to specialised computer programs, there are a number of resources that can be used to calculate sample size and assess the power of a study (see Useful Web sites).

In many studies, the two groups will have unequal sample sizes. In this situation, a two-sample t-test can still be used but in practice leads to a loss of statistical power, which may be important when the sample size is small. For example, a study with three times as many cases as controls and a total sample size of 100 participants (75 cases and 25 controls) has roughly the same statistical power as a balanced study with 76 participants (38 cases and 38 controls)[3]. Thus, the unbalanced study requires the recruitment of an extra 24 participants to achieve the same statistical power.

Research question

The data file **babies.sav** contains the information of birth length, birth weight and head circumference measured at 1 month of age in 256 babies. The babies were recruited during a population study in which one of the inclusion criteria was that the babies had to have been a term birth. The research question and null hypothesis are shown below. Unlike the null hypothesis, the research question usually specifies the direction of effect that is expected. Nevertheless, a two-tailed test should be used because the direction of effect could be in either direction and if the effect is in a direction that is not expected, it is usually important to know this especially in experimental studies. In this example, all three outcome measurements (birth length, birth weight and head circumference) are continuous and the explanatory measurement (gender) is a binary group variable.

Questions:	Are males longer than females? Are males heavier than females? Do males have a larger head circumference than females?
Null hypothesis:	There is no difference between males and females in length. There is no difference between males and females in weight. There is no difference between males and females in head circumference.
Variables:	Outcome variables = birth length, birth weight and head circumference (continuous) Explanatory variable = gender (categorical, binary)

The appropriate statistic that is used to test differences between groups is the *t* value. If the *t* value obtained from the two-sample *t*-test falls outside the *t* critical range and is therefore in the rejection region, the *P* value will be small and the null hypothesis will be rejected. In SPSS, the *P* value is calculated so it is not necessary to check statistical tables to obtain *t* critical values. When the null hypothesis is rejected, the conclusion is made that the difference between groups is statistically significant and did not occur by chance. It is important to remember that statistical significance does not only reflect the size of the difference between groups but also reflects the sample size. Thus, small unimportant differences between groups can be statistically significant when the sample size is large.

Statistical analyses

Before differences in outcome variables between groups can be tested, it is important that all of the assumptions specified in Box 3.1 are checked. In the data file **babies.sav**, the first assumption is satisfied because all the males are in one group (coded 1) and all the females are in a separate group (coded 2). In addition, each participant appears only once in their group, therefore the groups and the measurements are independent. All three outcome variables are on a continuous scale for each group, so the fourth assumption of the outcome variable being normally distributed must be tested. Descriptive statistics need to be obtained for the distribution of each outcome variable in each group rather than for the entire sample. It is also important to check for univariate outliers, calculate the effect size and test for homogeneity of variances. It is essential to identify outliers that tend to bias mean values of groups and make them more different or more alike than median values show they are.

Box 3.2 shows how to obtain the descriptive information for each group in SPSS.

Box 3.2 SPSS commands to obtain descriptive statistics

SPSS Commands

babies – SPSS Data Editor
    Analyze→Descriptive Statistics→Explore
Explore
    Highlight Birth weight, Birth length, and Head circumference and click into Dependent List
    Highlight Gender and click into Factor List
    Click on Plots
Explore: Plots
    Boxplots – Factor levels together (default setting)
    Descriptive – untick Stem and leaf (default setting), tick Histogram and tick Normality plots with tests
    Click Continue
Explore
    Click on Options
Explore: Options
    Missing Values – tick Exclude cases pairwise
    Click Continue
Explore
    Click OK

The Case Processing Summary table indicates that there are 119 males and 137 females in the sample and that none of the babies have missing values for any of the variables.

Explore

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	Gender	N	Percent	N	Percent	N	Percent
Birth weight (kg)	Male	119	100.0%	0	.0%	119	100.0%
	Female	137	100.0%	0	.0%	137	100.0%
Birth length (cms)	Male	119	100.0%	0	.0%	119	100.0%
	Female	137	100.0%	0	.0%	137	100.0%
Head circumference (cms)	Male	119	100.0%	0	.0%	119	100.0%
	Female	137	100.0%	0	.0%	137	100.0%

Descriptives

	Gender			Statistic	Std. error
Birth weight (kg)	Male	Mean		3.4430	0.03030
		95% confidence	Lower bound	3.3830	
		interval for mean	Upper bound	3.5030	
		5% trimmed mean		3.4383	
		Median		3.4300	
		Variance		0.109	
		Std. deviation		0.33057	
		Minimum		2.70	
		Maximum		4.62	
		Range		1.92	
		Inter-quartile range		0.4700	
		Skewness		0.370	0.222
		Kurtosis		0.553	0.440
	Female	Mean		3.5316	0.03661
		95% confidence	Lower bound	3.4592	
		interval for mean	Upper bound	3.6040	
		5% trimmed mean		3.5215	
		Median		3.5000	
		Variance		0.184	
		Std. deviation		0.42849	
		Minimum		2.71	
		Maximum		4.72	
		Range		2.01	
		Inter-quartile range		0.5550	
		Skewness		0.367	0.207
		Kurtosis		−0.128	0.411
Birth length (cm)	Male	Mean		50.333	0.0718
		95% confidence	Lower bound	50.191	
		interval for mean	Upper bound	50.475	
		5% trimmed mean		50.342	
		Median		50.500	
		Variance		0.614	
		Std. deviation		0.7833	
		Minimum		49.0	
		Maximum		51.5	
		Range		2.5	
		Inter-quartile range		1.000	
		Skewness		−0.354	0.222
		Kurtosis		−0.971	0.440
	Female	Mean		50.277	0.0729
		95% confidence	Lower bound	50.133	
		interval for mean	Upper bound	50.422	

Continued

	Gender			Statistic	Std. error
		5% trimmed mean		50.264	
		Median		50.000	
		Variance		0.728	
		Std. deviation		0.8534	
		Minimum		49.0	
		Maximum		52.0	
		Range		3.0	
		Inter-quartile range		1.500	
		Skewness		−0.117	0.207
		Kurtosis		−1.084	0.411
Head circumference (cm)	Male	Mean		34.942	0.1197
		95% confidence interval for mean	Lower bound	34.705	
			Upper bound	35.179	
		5% trimmed mean		34.967	
		Median		35.000	
		Variance		1.706	
		Std. deviation		1.3061	
		Minimum		31.5	
		Maximum		38.0	
		Range		6.5	
		Inter-quartile range		2.000	
		Skewness		−0.208	0.222
		Kurtosis		0.017	0.440
	Female	Mean		34.253	0.1182
		95% confidence interval for mean	Lower bound	34.019	
			Upper bound	34.486	
		5% trimmed mean		34.301	
		Median		34.000	
		Variance		1.914	
		Std. deviation		1.3834	
		Minimum		29.5	
		Maximum		38.0	
		Range		8.5	
		Inter-quartile range		1.500	
		Skewness		−0.537	0.207
		Kurtosis		0.850	0.411

The first check of normality is to compare the mean and median values provided by the Descriptives table and summarised in Table 3.1. The differences between the mean and median values are small for birth weight and relatively small for birth length and for head circumference.

Information from the Descriptives table indicates that the skewness and kurtosis values are all less than or close to ±1, suggesting that the data are

Table 3.1 Testing for a normal distribution

	Gender	Mean – median	Skewness (SE)	Skewness/SE (critical value)	Kurtosis (SE)	Kurtosis/SE (critical value)
Birth weight	Male	0.013	0.370 (0.222)	1.67	0.553 (0.440)	1.26
	Female	0.032	0.367 (0.207)	1.77	−0.128 (0.411)	−0.31
Birth length	Male	−0.167	−0.354 (0.222)	−1.59	−0.971 (0.440)	−2.21
	Female	0.277	−0.117 (0.207)	−0.57	−1.084 (0.411)	−2.64
Head circumference	Male	−0.058	−0.208 (0.222)	−0.94	0.017 (0.440)	0.04
	Female	0.253	−0.537 (0.207)	−2.59	0.850 (0.411)	2.07

approximately normally distributed. Calculations of normality statistics for skewness and kurtosis in Table 3.1 show that the critical values of kurtosis/SE for birth length for both males and females are less than −1.96 and outside the normal range, indicating that the distributions of birth length are relatively flat. The head circumference of females is negatively skewed because the critical value of skewness/SE is less than −1.96 and outside the normal range. Also, the distribution of head circumference for females is slightly peaked because the critical value of kurtosis/SE for this variable is outside the normal range of +1.96.

From the Descriptives table, it is possible to also compute effect sizes and estimate homogeneity of variances as shown in Table 3.2. The effect sizes using the pooled standard deviation are small for birth weight, very small for birth length and medium for head circumference. The variance of birth weight for females compared to males is 0.109:0.184 or 1:1.7. This indicates that females have a wider spread of birth weight scores, which is shown by similar minimum values for males and females (2.70 vs 2.71 kg) but a higher maximum value for females (4.62 vs 4.72 kg). For birth length and head circumference, males and females have similar variances with ratios of 1:1.12 and 1:1.1 respectively.

Table 3.2 Effect sizes and homogeneity of variances

	Difference in means and SD	Effect size (SD)	Maximum and minimum variance	Variance ratio
Birth weight	3.443 – 3.532/0.38	−0.23	0.184, 0.109	1:1.7
Birth length	50.33 – 50.28/0.82	0.06	0.728, 0.614	1:1.2
Head circumference	34.94 – 34.25/1.35	0.51	1.914, 1.706	1:1.1

Tests of Normality

		Kolmogorov–Smirnov[a]			Shapiro–Wilk		
	Gender	Statistic	*df*	Sig.	Statistic	*df*	Sig.
Birth weight (kg)	Male	0.044	119	0.200*	0.987	119	0.313
	Female	0.063	137	0.200*	0.983	137	0.094
Birth length (cm)	Male	0.206	119	0.000	0.895	119	0.000
	Female	0.232	137	0.000	0.889	137	0.000
Head circumference (cm)	Male	0.094	119	0.012	0.977	119	0.037
	Female	0.136	137	0.000	0.965	137	0.001

* This is a lower bound of the true significance.

[a] Lilliefors significance correction.

The Tests of Normality table shows that the distribution of birth weight for males and females is not significantly different from a normal distribution and therefore passes the test of normality. However, both the Kolmogorov–Smirnov and Shapiro–Wilk tests of normality indicate that birth length and head circumference for males and females are significantly different from a normal distribution.

The histograms shown in Figure 3.3 indicate that the data for birth weight of males and females follow an approximately normal distribution with one or two outlying values to the right hand side. The box plots shown in Figure 3.3 indicate that there is one outlying value for males and two outlying values for females that are 1.5 to 3 box lengths from the upper edge of the box. Both groups have outlying values at the high end of the data range that would tend to increase the mean value of each group. To check whether these outlying values are univariate outliers, the mean of the group is subtracted from the outlying value and then divided by the standard deviation of the group. This calculation converts the outlying value to a z score. If the absolute value of the z score is greater than 3, then the value is a univariate outlier[4]. If the sample size is very small, then an absolute z score greater than 2 should be considered to be a univariate outlier[4].

For the birth weight of males, the outlying value is the maximum value of 4.62 and is case 249. By subtracting the mean from this value and dividing by the standard deviation that is $((4.62 - 3.44)/0.33)$, a z value of 3.58 is obtained indicating that case 249 is a univariate outlier. This score is an extreme value compared to the rest of the data points and should be checked to ensure that it is not a transcribing or data entry error. Checking shows that the score was entered correctly and came from a minority ethnic group. There is only one univariate outlier and the sample size is large and therefore it is unlikely that this outlier will have a significant influence on the summary statistics. If the sample size is large, say at least 100 cases, then a few cases with z scores greater than the absolute value of 3 would be expected by chance[4].

If there were more than a few univariate outliers, a technique that can be used to reduce the influence of outliers is to transform the scores so that the shape of the distribution is changed. The outliers will still be present on the tails of the transformed distribution, but their influence will be reduced[5]. If there are only a few outliers, another technique that can be used is to change the score for the outlier so it is not so extreme, for example by changing the score to one point larger or smaller than the next extreme value in the distribution[5].

For illustrative purposes, the case that is a univariate outlier for birth weight of males will be changed so that it is less extreme. Using the *Analyze → Descriptive Statistics → Explore* commands and requesting outliers as shown in Box 2.2 the next extreme value is obtained, which is case 149 with a value of 4.31. If a value of 1 were added to the next extreme value this would give a value of 5.31, which would be the changed value for the univariate outlier, case 249. However, this value is higher than the actual value of case 249, therefore this technique is not suitable. An alternative is that the univariate outlier is changed to a value that is within three z scores of the mean. For birth weight

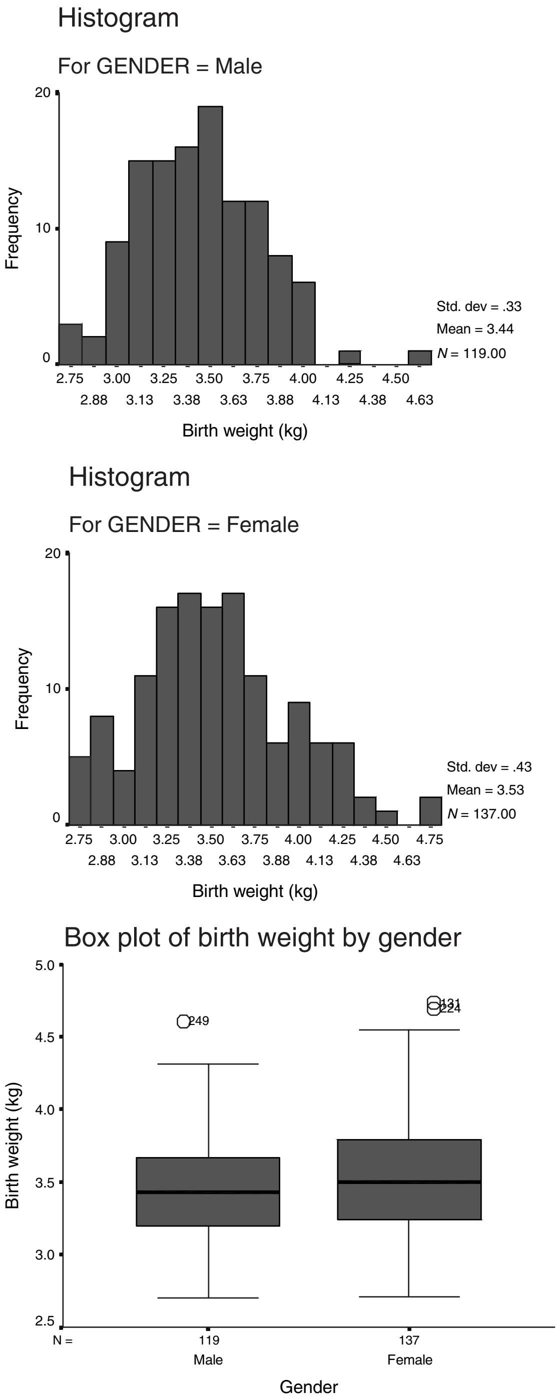

Figure 3.3 Plots of birth weight by gender.

of males, this value would be 4.43 that is (0.33 × 3) + 3.44. This value is lower than the present value of case 249 and slightly higher than the next extreme value, case 149. Therefore, the value of case 249 is changed from 4.62 to 4.43. This information should be recorded in the study handbook and the method recorded in any publications.

After the case has been changed, the Descriptives table for birth weight of males should be obtained with new summary statistics. This table shows that the new maximum value for birth weight is 4.43. The mean of 3.4414 is almost the same as the previous mean of 3.4430, and the standard deviation, skewness and kurtosis values of the group have slightly decreased, indicating a slightly closer approximation to a normal distribution.

Descriptives

	Gender			Statistic	Std. error
Birth weight (kg)	Male	Mean		3.4414	0.02982
		95% confidence interval for mean	Lower bound	3.3824	
			Upper bound	3.5005	
		5% trimmed mean		3.4383	
		Median		3.4300	
		Variance		0.106	
		Std. deviation		0.32525	
		Minimum		2.70	
		Maximum		4.43	
		Range		1.73	
		Inter-quartile range		0.4700	
		Skewness		.235	0.222
		Kurtosis		.028	0.440
	Female	Mean		3.5316	0.03661
		95% confidence interval for mean	Lower bound	3.4592	
			Upper bound	3.6040	
		5% trimmed mean		3.5215	
		Median		3.5000	
		Variance		0.184	
		Std. deviation		0.42849	
		Minimum		2.71	
		Maximum		4.72	
		Range		2.01	
		Inter-quartile range		0.5550	
		Skewness		0.367	0.207
		Kurtosis		−0.128	0.411

For the birth weight of females, cases 131 and 224 are outlying values and are also from the same minority ethic group as case 249. Case 131 is the higher of the two values and is the maximum value of the group with a value of 4.72, which is 2.77 standard deviations above the group mean and is not a univariate outlier. Therefore, case 224 is not a univariate outlier and the values of both cases 131 and 224 are retained.

Another alternative to transforming data or changing the values of univariate outliers is to omit the outliers from the analysis. If there were more univariate outliers from the same minority ethnic group, the data points could be included so that the results could be generalised to all ethnic groups in the recruitment area. Alternatively, all data points from the minority group could be omitted regardless of outlier status although this would limit the generalisability of the results.

The decision of whether to omit or include outlying values is always difficult. If the sample was selected as a random sample of the population, omission of some participants from the analyses should not be considered.

The histograms shown in Figure 3.4 indicate that birth length of males and females does not follow a classic normal distribution and explains the kurtosis statistics for males and females in the Descriptives table. The birth length of both males and females has a narrow range of only 49 to 52 cm as shown in the Descriptives table. The histograms show that birth length is usually recorded to the nearest centimetre and rarely to 0.5 cm (Figure 3.4). This rounding of birth length may be satisfactory for obstetric records but it would be important to ensure that observers measure length to an exact standard in a research study. Since birth length has only been recorded to the nearest centimetre, summary statistics for this variable should be reported using no more than one decimal place.

The box plots shown in Figure 3.4 confirm that females have a lower median birth length than males but have a wider absolute range of birth length values as indicated by the length of the box. This suggests that the variances of each group may not be homogeneous.

The histograms for head circumference shown in Figure 3.5 indicate that the data are approximately normally distributed although there is a slight tail to the left for females. This is confirmed by the box plot in Figure 3.5 that shows a few outlying values at the lower end of the distribution, indicating that a few female babies have a head circumference that is smaller than most other babies in the group. The smallest value is case 184 with a head circumference of 29.5, which has a z score of 3.44 and is a univariate outlier. The next smallest value is case 247 with a value of 30.2, which has a z score of 2.93. There is only one univariate outlier, which is expected in this large sample as part of normal variation. It is unlikely that this one outlier will have a significant impact on summary statistics, so it is not adjusted and is included in the data analyses. The maximum value for head circumference of females is case 108 with a value of 38, which has a z value of 2.71 and is not a univariate outlier.

Finally, after the presence of outliers has been assessed and all tests of normality have been conducted, the tests of normality can be summarised as shown in Table 3.3. In the table, 'yes' indicates that the distribution is within the normal range and 'no' indicates that the distribution is outside the normal range.

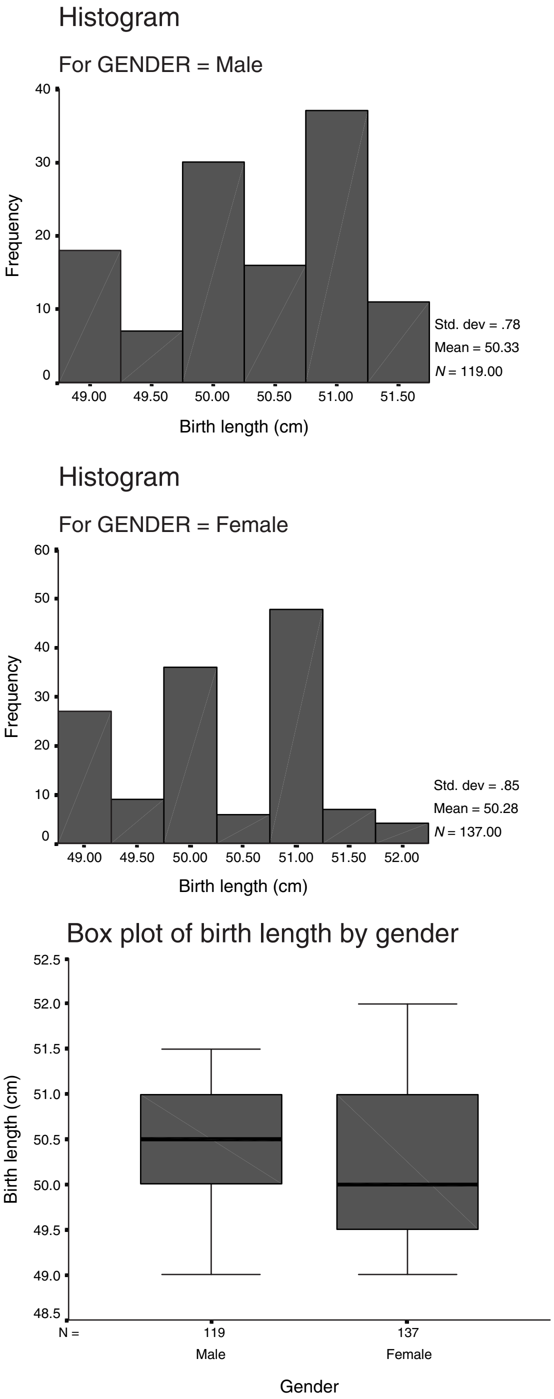

Figure 3.4 Plots of birth length by gender.

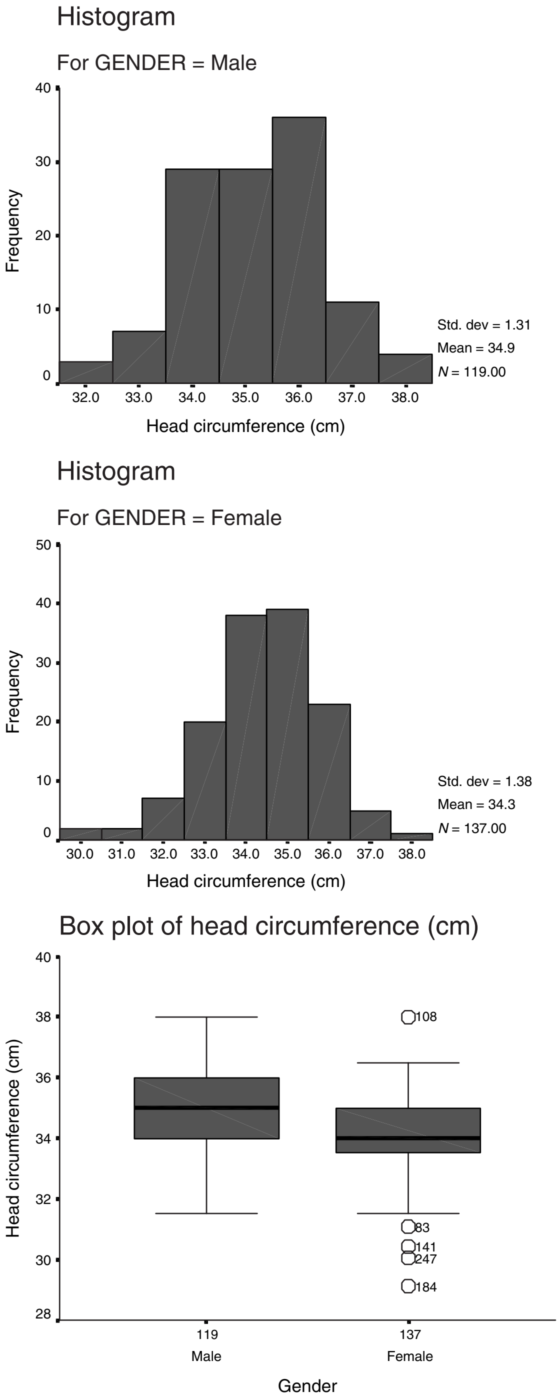

Figure 3.5 Plots of head circumference by gender.

Table 3.3 Summary of whether descriptive statistics indicates a normal distribution in each group

		Mean – median	Skewness	Kurtosis	K-S test	Plots	Overall decision
Birth weight	Males	Yes	Yes	Yes	Yes	Yes	Yes
	Females	Yes	Yes	Yes	Yes	Yes	Yes
Birth length	Males	Yes	Yes	No	No	No	Yes
	Females	Probably	Yes	No	No	No	Yes
Head circumference	Males	Yes	Yes	Yes	No	Yes	Yes
	Females	Probably	No	No	No	Yes	Yes

Based on all checks of normality, the birth weight of males and females is normally distributed so a two-sample *t*-test can be used. The distribution of birth length of males and females has a flat shape but does not have any outliers. While birth length of both males and females has some kurtosis, this has less impact on summary statistics than if the data were skewed. The variable head circumference is normally distributed for males but for females has some slight skewness caused by a few outlying values. However, the mean and median values for females are not largely different. Also, in the female group there is only one outlier and the number of outlying values is small and the sample size is large, and a *t*-test will be robust to these small deviations from normality. Therefore, the distribution of each outcome variable is approximately normally distributed for both males and females, and a two-sample *t*-test can be used to test between group differences.

Two-sample *t*-test

A two-sample *t*-test is basically a test of how different two group means are in terms of their variance. Clearly, if there was no difference between the groups, the difference to variance ratio would be close to zero. The *t* value becomes larger as the difference between the groups increases in respect to their variances. An approximate formula for calculating a *t* value, when variances are equal is:

$$t = (x_1 - x_2)/\surd({s_p}^2/n_1 + {s_p}^2/n_2)$$

where x is the mean, ${s_p}^2$ is the pooled variance and n is the sample size of each group. Thus, t is the difference between the mean values for the two groups divided by the standard error of the difference. When variances of the two groups are not equal, that is Levene's test for equality of variances is significant, individual group variances and not the pooled variance are used in calculating the t value. Box 3.3 shows the SPSS commands to obtain a two-sample *t*-test in which the numbered coding for each group has to be entered.

Box 3.3 SPSS commands to obtain a two-sample *t*-test

SPSS Commands

babies – SPSS Data Editor

Analyze → Compare Means → Independent Samples T Test

Independent-Samples T-Test

Highlight Birth weight, Birth length and Head circumference and click into Test Variable(s)

Highlight Gender and click into Group Variable

Click on Define Groups

Define Groups

Enter coding: 1 for Group 1 and 2 for Group 2

Click Continue

Independent-Samples T-Test

Click OK

T-Test

Group Statistics

	Gender	***N***	**Mean**	**Std. deviation**	**Std. error mean**
Birth weight (kg)	Male	119	3.4414	0.32525	0.02982
	Female	137	3.5316	0.42849	0.03661
Birth length (cm)	Male	119	50.333	0.7833	0.0718
	Female	137	50.277	0.8534	0.0729
Head circumference (cm)	Male	119	34.942	1.3061	0.1197
	Female	137	34.253	1.3834	0.1182

The first Group Statistics table shows summary statistics, which are identical to the statistics obtained in *Analyze → Descriptive Statistics → Explore*. However, there is no information in this table that would allow the normality of the distributions in each group or the presence of influential outliers to be assessed. Thus, it is important to always obtain full descriptive statistics to check for normality prior to conducting a two-sample *t*-test.

In the Independent Samples Test table (p. 70), the first test is Levene's test of equal variances. A *P* value for this test that is less than 0.05 indicates that the variances of the two groups are significantly different and therefore that the *t* statistics calculated assuming variances are not equal should be used. The variable birth weight does not pass the test for equal variances with a *P* value of 0.007 but this was expected because the statistics in the Descriptives table showed a 1:1.7, or almost two-fold, difference in variance (Table 3.2). For this variable, the statistics calculated assuming variances are not equal is appropriate. However, both birth length and head circumference pass the test

Independent Samples Test

		Levene's test for equality of variances		*t*-test for equality of means					95% confidence interval of the difference	
		F	Sig.	*t*	*df*	Sig. (Two-tailed)	Mean difference	Std. error difference	Lower	Upper
Birth weight (kg)	Equal variances assumed	7.377	0.007	−1.875	254	0.062	−0.0902	0.04812	−0.18498	0.00455
	Equal variances not assumed			−1.911	249.659	0.057	−0.0902	0.04721	−0.18320	0.00277
Birth length (cm)	Equal variances assumed	2.266	0.133	0.538	254	0.591	0.055	0.1030	−0.1473	0.2581
	Equal variances not assumed			0.541	253.212	0.589	0.055	0.1023	−0.1461	0.2569
Head circumference (cm)	Equal variances assumed	0.257	0.613	4.082	254	0.000	0.689	0.1689	0.3568	1.0221
	Equal variances not assumed			4.098	252.221	0.000	0.689	0.1682	0.3581	1.0208

of equal variances and the differences between genders can be reported using the t statistics that have been calculated assuming equal variances.

For birth weight, the appropriate t statistic can be read from the line *Equal variances not assumed*. The t statistic for birth length and head circumference can be read from the line *Equal variances assumed*. The t-test P value indicates the likelihood that the differences in mean values occurred by chance. If the likelihood is small, that is less than 0.05, the null hypothesis can be rejected. For birth weight, the P value for the difference between the genders does not reach statistical significance with a P value of 0.057. This P value indicates that there is a 5.7%, or 57 in 1000, chance of finding this difference if the two groups in the population have equal means.

For birth length, there is clearly no difference between the genders with a P value of 0.591. For head circumference, there is a highly significant difference between the genders with a P value of <0.0001. The head circumference of female babies is significantly lower than the head circumference of male babies. This P value indicates that there is less than a 1 in 1000 chance of this difference being found by chance if the null hypothesis is true.

Confidence intervals

Confidence intervals are invaluable statistics for estimating the precision around a summary statistic such as a mean value and for estimating the magnitude of the difference between two groups. For mean values, the 95% confidence interval is calculated as follows:

$$\text{Confidence interval (CI)} = \text{Mean} \pm (1.96 \times \text{SE})$$

where SE = standard error.

Thus, using the data from the Group Statistics table provided in the SPSS output for a t-test, the confidence interval for birth weight for males would be calculated as follows:

$$95\% \text{ confidence interval} = 3.441 \pm (1.96 \times 0.0298) = 3.383, 3.499$$

These values correspond to the 95% confidence interval lower and upper bounds shown in the Descriptives table. To calculate the 99% confidence interval, the critical value of 2.57 instead of 1.96 would be used in the calculation. This would give a wider confidence interval that would indicate the range in which the true population mean lies with more certainty.

The confidence intervals of two groups can be used to assess whether there is a significant difference between the two groups. If the 95% confidence interval of one group does not overlap with the confidence interval of another, there will be a statistically significant difference between the two groups. The interpretation of the overlapping of confidence intervals when two groups are compared is shown in Table 3.4.

Table 3.4 Interpretation of 95% confidence intervals

Relative position of confidence intervals	Statistical significance between groups
Do not overlap	Highly significant difference
Overlap, but one summary statistic is not within the confidence interval for the other	Possibly significant, but not highly
Overlap to a large extent	Definitely not significant

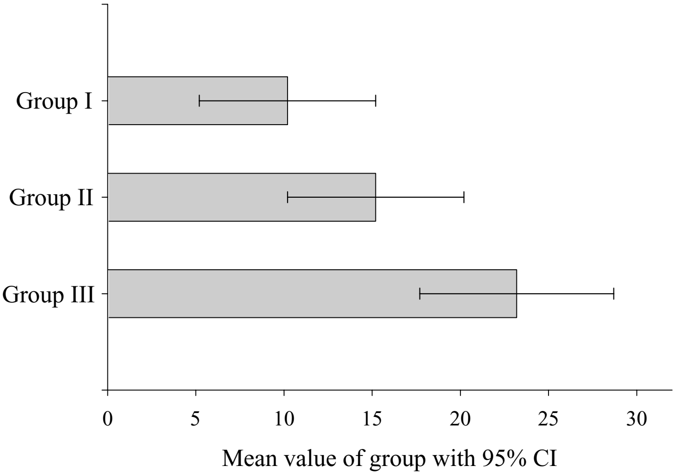

Figure 3.6 Interpretation of the overlap between 95% confidence intervals.

Figure 3.6 shows the mean values of an outcome measurement, say per cent change from baseline, in three independent groups. The degree of overlap of the confidence intervals reflects the P values. For the comparison of group I vs III the confidence intervals do not overlap and the group means are significantly different at $P < 0.0001$. For the comparison of group I vs II, the confidence intervals overlap to a large extent and the group means are not significantly different at $P = 0.52$. For the comparison of group II vs III, where one summary statistic is not within the confidence interval of the other group, the difference between group means is marginally significant at $P = 0.049$.

In the data set, **babies.sav** the means and confidence intervals of the outcome variable for each group can be summarised as shown in Table 3.5. The overlap of the 95% confidence intervals confirms the between group P values.

Finally, in the Independent Samples Test table, the mean difference and its 95% confidence interval were also reported. The mean difference is the absolute difference between the mean values for males and females. The direction of the mean difference is determined by the coding used for gender. With males coded as 1 and females as 2, the differences are represented as males – females. Therefore, this section of the table indicates that males have a mean

Table 3.5 Summary of mean values and interpretation of 95% confidence intervals

	Mean (95% CI) Males	Mean (95% CI) Females	Overlap of CI	Significance
Birth weight	3.44 (3.38, 3.50)	3.53 (3.46, 3.60)	Slight	$P = 0.06$
Birth length	50.3 (50.1, 50.5)	50.3 (50.1, 50.4)	Large	$P = 0.59$
Head circumference	34.9 (34.7, 35.2)	34.3 (34.0, 34.5)	None	$P < 0.0001$

birth weight that is 0.0902 kg lower than females but a mean birth length that is 0.055 cm longer and a mean head circumference that is 0.689 cm larger than females.

Obviously, a zero value for mean difference would indicate no difference between groups. Thus, a 95% confidence interval around the mean difference that contains the value of zero, as it does for birth length, suggests that the two groups are not significantly different. A confidence interval that is shifted away from the value of zero, as it is for head circumference, indicates with 95% certainty that the two groups are different. The slight overlap with zero for the 95% confidence interval of the difference for birth weight reflects the marginal *P* value.

Reporting the results in a table

The results from two-sample *t*-tests can be reported as shown in Table 3.6. In addition to reporting the *P* value for the difference between genders, it is important to report the characteristics of the groups in terms of their mean values and standard deviations, the effect size and the mean between group difference and 95% confidence interval. Except for effect size, these statistics are all provided on the SPSS *t*-test output.

Table 3.6 Summary of birth details by gender

	Males Mean (SD)	Females Mean (SD)	Effect size (SD)	Mean difference and 95% CI	*P* value
Birth weight (kg)	3.44 (0.33)	3.53 (0.43)	−0.23	−0.09 (−0.18, −0.003)	0.06
Birth length (cm)	50.3 (0.78)	50.3 (0.85)	0.06	0.06 (−0.15, 0.26)	0.59
Head circumference (cm)	34.9 (1.31)	34.3 (1.38)	0.51	0.69 (0.36, 1.02)	<0.0001

The *P* values show the significance of the differences, but the effect size and mean difference give an indication of the magnitude of the differences between the groups. As such, these statistics give a meaningful interpretation to the *P* values.

Reporting results in a graph

Graphs are important tools for conveying the results of research studies. The most informative figures are clear and self-explanatory. For mean values from continuous data, dot plots are the most appropriate graph to use. In summarising data from continuous variables, it is important that bar charts are only used when the distance from zero has a meaning and therefore when the zero value is shown on the axis.

Box 3.4 shows how to draw a dot plot with error bars in SPSS.

Box 3.4 SPSS commands to draw a dot plot

SPSS Commands

babies – SPSS Data Editor

  Graphs → Error Bar

Error Bar

  Click Simple

  Click Define

Define Simple Error Bar: Summaries for Groups of Cases

  Highlight Birth weight and click into Variable

  Highlight Gender and click into Category Axis

  Click OK

The commands in Box 3.4 can then be repeated for birth length and head circumference to produce the graphs shown in Figure 3.7. Note that the scales on the *y*-axis of the three graphs shown in Figure 3.7 are different and therefore it is not possible to compare the graphs with one another or combine them.

However, in each graph shown in Figure 3.7, the degree of overlap of the confidence intervals provides an immediate visual image of the differences between genders. The graphs show that female babies are slightly heavier with a small overlap of 95% confidence intervals and that they are not significantly shorter because there is a large overlap of the 95% confidence intervals. However, males have a significantly larger head circumference because there is no overlap of confidence intervals. The extent to which the confidence intervals overlap in each of the three graphs provides a visual explanation of the *P* values obtained from the two-sample *t*-tests.

Drawing a figure in SigmaPlot

For publication quality, the differences between groups can be presented in a graph using SigmaPlot. In the example below, only the data for head circumference are plotted but the same procedure could be used for birth weight and length. First, the width of confidence interval has to be calculated using the Descriptives table obtained from *Analyze → Descriptive Statistics → Explore*.

Width of 95% CI = Mean − Lower bound of 95% CI

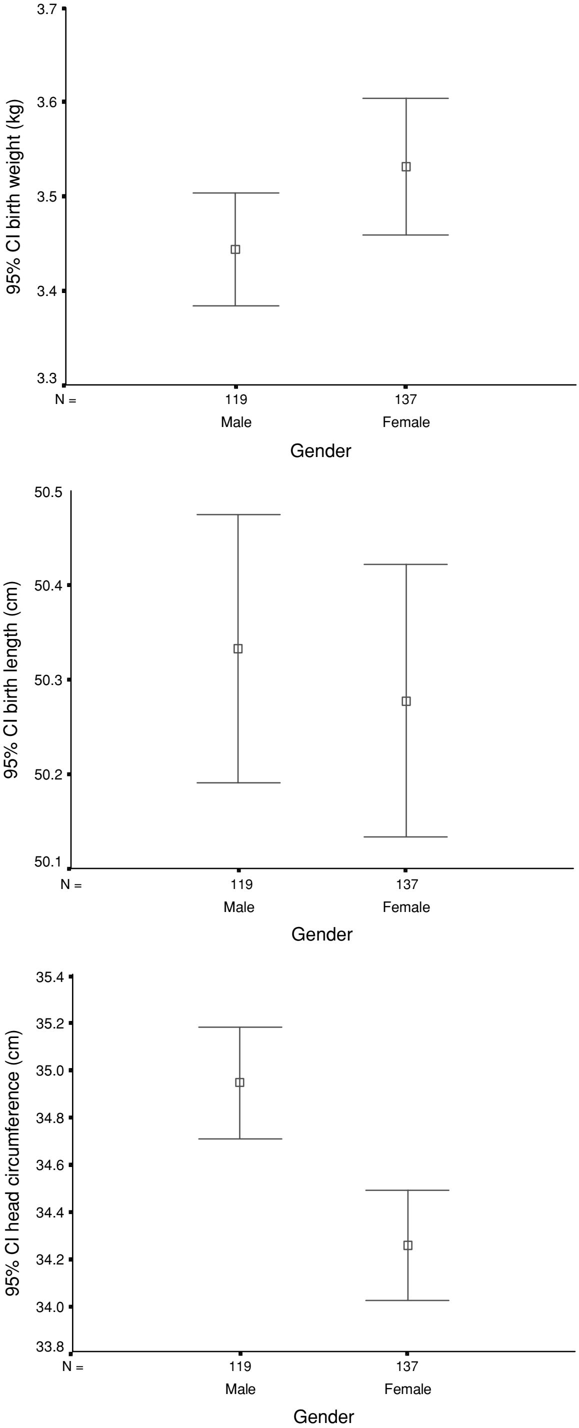

Figure 3.7 Dot plots of birth weight, birth length and head circumference by gender.

Thus, the width of the confidence interval for head circumference is as follows:

$$\text{Width of 95\% CI} = 34.94 - 34.71 = 0.23 \text{ (males)}$$
$$= 34.25 - 34.02 = 0.23 \text{ (females)}$$

The numerical values of the mean and the width of the 95% confidence interval are then entered into the SigmaPlot spreadsheet as follows and the commands in Box 3.5 can be used to draw a dot plot as shown in Figure 3.8.

Column 1	Column 2
34.94	0.23
34.25	0.23

Box 3.5 SigmaPlot commands for drawing a dot plot

SigmaPlot Commands

SigmaPlot – [Data 1]*
Graph → Create Graph
Create Graph – Type
    Highlight Scatter Plot, click Next
Create Graph –Style
    Highlight Simple Error Bars, click Next
Create Graph – Error Bars
    Symbol Values = Worksheet Columns (default), click Next
Create Graph – Data Format
    Highlight Single Y, click Next
Create Graph – Select Data
    Data for Y = use drop box and select Column 1
    Data for Error = use drop box and select Column 2,
    Click Finish

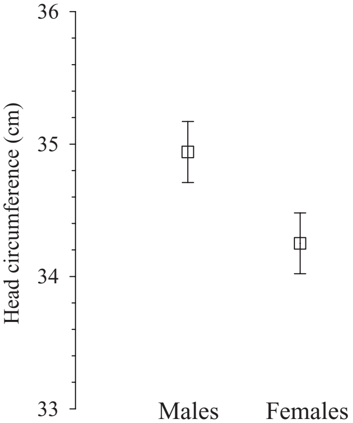

Figure 3.8 Mean head circumference at 1 month by gender.

Once the plot is obtained, the graph can be customised by changing the axes, axis labels, graph colours, etc. using options under the menu *Graph → Graph Properties*.

Alternatively, the absolute mean differences between males and females could be presented in a graph. Birth length and head circumference were measured in the same scale (cm) and therefore can be plotted on the same figure. Birth weight is in different units (kg) and would need to be presented in a different figure.

The width of the confidence intervals is calculated from the mean difference and lower 95% confidence interval of the difference, as follows:

$$\text{Width of 95\% CI for birth length} = 0.055 - (-0.147) = 0.202$$

$$\text{Width of 95\% CI for head circumference} = 0.689 - 0.357 = 0.332$$

These values are then entered into the SigmaPlot spreadsheet as follows:

Column 1	Column 2
0.055	0.202
0.689	0.332

Box 3.6 shows how a horizontal scatter plot can be drawn in SigmaPlot to produce Figure 3.9. The decision whether to draw horizontal or vertical dot plots is one of personal choice; however, horizontal plots have the advantage that longer descriptive labels can be included in a way that they can be easily read.

Box 3.6 SigmaPlot commands for horizontal dot plot

SigmaPlot Commands

SigmaPlot – [Data 1]*
Graph →Create Graph
Create Graph – Type
    Highlight Scatter Plot, click Next
Create Graph – Style
    Highlight Horizontal Error Bars, click Next
Create Graph – Error Bars
    Symbol Values = Worksheet Columns (default), click Next
Create Graph – Data Format
    Highlight Many X, click Next
Create Graph – Select Data
    Data for X1 = use drop box and select Column 1
    Data for Error 1 = use drop box and select Column 2
Click Finish

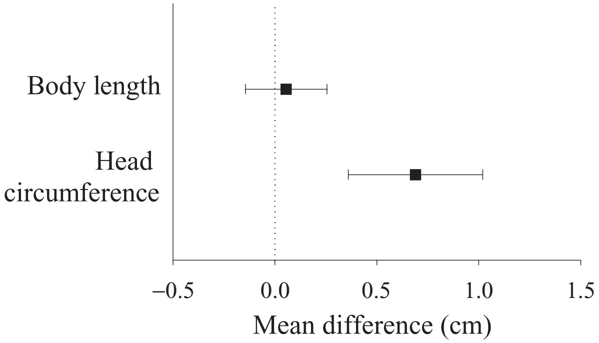

Figure 3.9 Mean difference in body length and head circumference between males and females at 1 month of age.

Rank based non-parametric tests

Rank based non-parametric tests are used when the data do not conform to a normal distribution. If the data are clearly skewed, if outliers have an important effect on the mean value or if the sample size in one or more of the groups is small, say between 20 and 30 cases, then a rank based non-parametric test should probably be used. These tests rely on ranking and summing the scores in each group and may lack sufficient power to detect a significant difference between two groups when the sample size is very small.

The non-parametric test that is equivalent to a two-sample *t*-test is the Mann–Whitney U test, which the Wilcoxon rank sum produces the same result as W test. The Mann–Whitney U test is based on the ranking of measurements from two samples to estimate whether the samples are from the same population. In this test, no assumptions are made about the distribution of the measurements in either group.

The assumptions for the Mann–Whitney U test are shown in Box 3.7.

Box 3.7 Assumptions for Mann–Whitney U test to compare two independent samples

The assumptions for the Mann–Whitney U test are:
- the data are randomly sampled from the population
- the groups are independent, that is each participant is in one group only

Research question

The spreadsheet **surgery.sav**, which was used in Chapter 2, contains the data for 141 babies who attended hospital for surgery, their length of stay and whether they had an infection during their stay.

Question: Do babies who have an infection have a longer stay in hospital?

Null hypothesis: That there is no difference in length of stay between babies who have an infection and babies who do not have an infection

Variables: Outcome variable = length of stay (continuous)
Explanatory variable = infection (categorical, binary)

Statistical analyses

Descriptive statistics and the distribution of the outcome variable length of stay in each group can be inspected using the commands shown in Box 3.2 with length of stay as the dependent variable and infection as the factor.

Infection

Descriptives

	Infection			Statistic	Std. error
Length of stay	No	Mean		33.20	3.706
		95% confidence interval for mean	Lower bound	25.82	
			Upper bound	40.58	
		5% trimmed mean		28.25	
		Median		22.50	
		Variance		1098.694	
		Std. deviation		33.147	
		Minimum		0	
		Maximum		244	
		Range		244	
		Inter-quartile range		19.75	
		Skewness		4.082	0.269
		Kurtosis		21.457	0.532
	Yes	Mean		45.52	5.358
		95% confidence interval for mean	Lower bound	34.76	
			Upper bound	56.28	
		5% trimmed mean		40.36	
		Median		37.00	
		Variance		1492.804	
		Std. deviation		38.637	
		Minimum		11	
		Maximum		211	
		Range		200	
		Inter-quartile range		28.50	
		Skewness		2.502	0.330
		Kurtosis		7.012	0.650

Continued

Tests of Normality

		Kolmogorov–Smirnov[a]			Shapiro–Wilk		
	Infection	Statistic	*df*	Sig.	Statistic	*df*	Sig.
Length of stay	No	0.252	80	0.000	0.576	80	0.000
	Yes	0.262	52	0.000	0.707	52	0.000

[a] Lilliefors significance correction.

The Descriptives table shows that the mean and median values for length of stay for babies with no infection are 33.20 – 22.50, or 10.70 units apart and 45.52 – 37.00, or 8.52 units apart for babies with an infection. The variances are unequal at 1098.694 for no infection and 1492.804 for infection, that is a ratio of 1:1.4. The skewness statistics are all above 2 and the kurtosis statistics are also high, indicating that the data are peaked and are not normally distributed. The *P* values for the Kolmogorov–Smirnov and the Shapiro–Wilk tests are shown in the column labelled Sig. and are less than 0.05 for both groups, indicating that the data do not pass the tests of normality in either group.

The histograms and plots shown in Figure 3.10 confirm the results of the tests of normality. The histograms show that both distributions are positively skewed with tails to the right. The Q–Q plot for each group does not follow the line of normality and is significantly curved. The box plots show a number of extreme and outlying values. The maximum value for length of stay of babies with no infection is 6.36 *z* scores above the mean, while for babies with an infection the maximum value is 4.28 *z* scores above the mean.

The normality statistics for babies with an infection and babies without an infection are summarised in Table 3.7, with 'no' indicating that the distribution is outside the normal range.

For both groups, the data are positively skewed and could possibly be transformed to normality using a logarithmic transformation. Without transformation, the most appropriate test for analysing length of stay is a rank based non-parametric test, which can be obtained using the commands shown in Box 3.8.

The Mann–Whitney U test is based on ranking the data values as if they were from a single sample. For illustrative purposes, a subset of the data, that is the first 20 cases in the data set with valid length of stay are shown in Table 3.8. Firstly, the data are sorted in order of magnitude and ranked. Data points that are equal share tied ranks. Thus, the two data points of 13 share the ranks of 7 and 8 and are rated at 7.5 each. Similarly, the four data points of 17 share the ranks from 17 to 20 and are ranked at 18.5 each, which is the mean of the four rankings. Once the ranks are assigned, they are then summed for each of the groups.

In SPSS, the mean rank and the sum of the ranks are calculated for each group. In the Ranks table all cases are included. The sum of ranks and mean ranks gives a direction of effect but because the data are ranked, the dimension is different from the original measurement and is therefore difficult to communicate. The Mann–Whitney U and the Wilcoxon W that are obtained from SPSS are two derivations of the same test and are best reported as the Mann–Whitney U test. The Test Statistics table shows that the P value for the difference between groups is $P = 0.004$ which is statistically significant. The asymptotic significance value is reported when the sample size is large, say more than 30 cases, otherwise the *Exact* button at the bottom of the command screen can be used to calculate P values for a small sample.

The difference between the groups could be reported in a table as shown in Table 3.9.

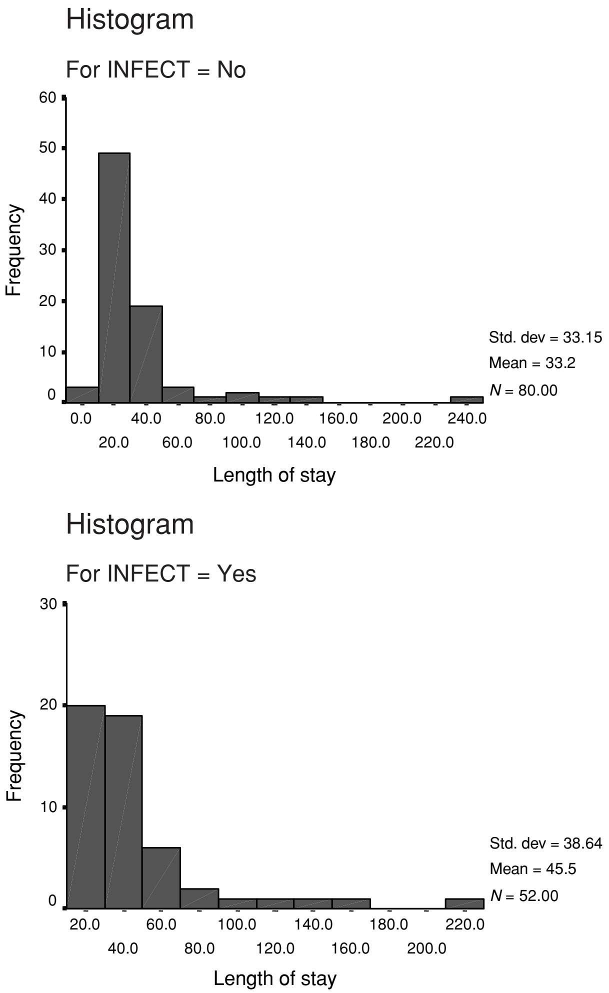

Figure 3.10 Plots of length of stay by infection.

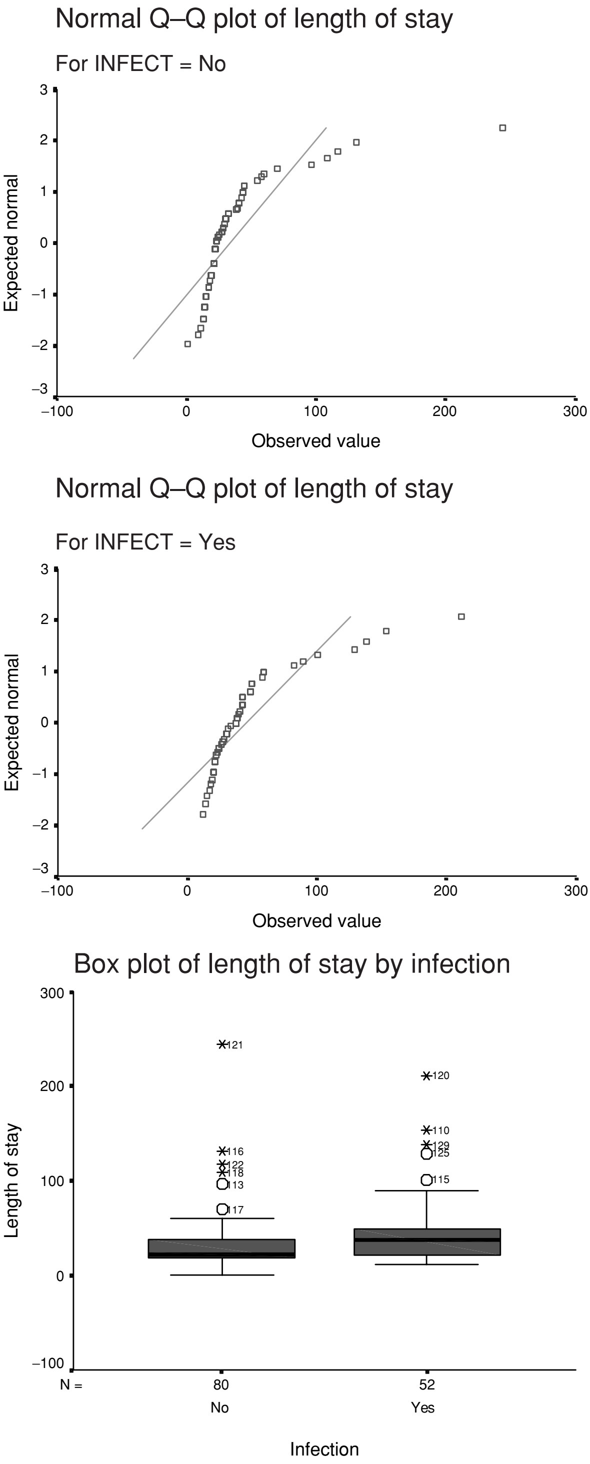

Figure 3.10 *Continued*

Table 3.7 Summary of statistics to assess whether data are within normal limits or outside normal range

Group	Mean – median	Skewness	Kurtosis	Shapiro–Wilk test	K-S test	Plots	Overall decision
No	No	No	No	No	No	No	No
Yes	No	No	No	No	No	No	No

Box 3.8 SPSS commands to obtain a non-parametric test for two independent groups

SPSS Commands

```
surgery – SPSS Data Editor
        Analyze → Nonparametric Tests → 2 Independent Samples
Two-Independent-Samples Test
        Highlight Length of stay into Test Variable List
        Highlight Infection into Grouping Variable
        Test Type tick Mann-Whitney U (default setting)
        Click on Define Groups
Two Independent Samples: Define Groups
        Group1 = 1
        Group 2 = 2
        Click Continue
Two-Independent-Samples Test
        Click OK
```

NPar Tests
Mann–Whitney Test

Ranks

	Infection	*N*	Mean rank	Sum of ranks
Length of stay	No	80	58.88	4710.00
	Yes	52	78.23	4068.00
	Total	132		

Test Statistics[a]

	Length of stay
Mann–Whitney U	1470.000
Wilcoxon W	4710.000
Z	−2.843
Asymp. sig. (two-tailed)	0.004

[a] Grouping variable: infection.

Table 3.8 Ranking data to compute non-parametric statistics

ID	Length of stay	Infection group	Rank Group 1	Rank Group 2
32	0	1	1	
33	1	1	2	
12	9	1	3	
16	11	1	4.5	
22	11	2		4.5
28	12	2		6
20	13	1	7.5	
27	13	1	7.5	
10	14	1	10.5	
11	14	1	10.5	
24	14	1	10.5	
25	14	2		10.5
14	15	1	14.5	
19	15	1	14.5	
23	15	2		14.5
30	15	1	14.5	
13	17	1	18.5	
15	17	1	18.5	
17	17	1	18.5	
21	17	2		18.5
		Sum of ranks	156	54
		N	15	5
		Mean	10.5	10.8

Another approach to non-normal data is to divide the outcome variable into categorical centile groups as discussed in Chapter 7. Decision about whether to use non-parametric tests, to transform the variable or to categorise the values requires careful consideration. The decision should be based on the size of the sample, the effectiveness of the transformation in normalising the data and the ways in which the relationship between the explanatory and outcome variables is best presented.

Notes for critical appraisal

Questions to ask when assessing descriptive statistics published in the literature are shown in Box 3.9.

Table 3.9 Length of stay for babies with infection and without infection

	Infection absent	Infection present	*P* value
Number			
Length of stay	80	52	
Median and IQ range	22.50 (19.75)	45.52 (37.00)	0.004

Box 3.9 Questions for critical appraisal

The following questions should be asked when appraising published results:

- are any cases included in a group more than once, for example are any follow-up data treated as independent data?
- is there evidence that the outcome variable is normally distributed in each group?
- if the variance of the two groups is unequal, has the correct *P* value, that is the *P* value with equal variances not assumed, been reported?
- are the summary statistics appropriate for the distributions?
- are there any influential outliers that could have increased the difference in mean values between the groups?
- Are mean values presented appropriately in figures as dot plots or are histograms used inappropriately?
- are mean values and the differences between groups presented with 95% confidence intervals?

References

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CHAPTER 4

Continuous variables: paired and one-sample *t*-tests

A statistician is a person who likes to prove you wrong, 5% of the time.
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Objectives

The objectives of this chapter are to explain how to:
- analyse paired or matched data
- use paired *t*-tests and one-sample *t*-tests
- interpret results from non-parametric paired tests
- report changes or differences in paired data in appropriate units

In addition to two-sample (independent) *t*-tests, there are also two other *t*-tests that can be used to analyse continuous data, that is paired *t*-tests and one-sample (single sample) *t*-tests. All three types of *t*-test can be one-tailed or two-tailed tests but one-tailed *t*-tests are rarely used.

A paired *t*-test is used to estimate whether the means of two related measurements are significantly different from one another. This test is used when two continuous variables are related because they are collected from the same participant at different times, from different sites on the same person at the same time or from cases and their matched controls[1]. Examples of paired study designs are:

- data from a longitudinal study
- measurements collected before and after an intervention in an experimental study
- differences between related sites in the same person, for example limbs, eyes or kidneys
- matched cases and controls

For a paired *t*-test, there is no explanatory (group) variable. The outcome of interest is the difference in the outcome measurements between each pair or between each case and its matched control, that is the within-pair differences. When using a paired *t*-test, the variation between the pairs of measurements is the most important statistic and the variation between the participants, as when using a two-sample *t*-test, is of little interest. In effect, a paired *t*-test is used to assess whether the mean of the differences between the two related measurements is significantly different from zero.

For related measurements, the data for each pair of values must be entered on the same row of the spreadsheet. Thus, the number of rows in the data sheet is the same as the number of participants when the outcome variable is measured twice for each participant or is the number of participant-pairs when cases and controls are matched. When each participant is measured on two occasions, the effective sample size is the number of participants. In a matched case-control study, the number of case-control pairs is the effective sample size and not the total number of participants. For this reason, withdrawals, loss of follow-up data and inability to recruit matched controls reduce both power and the generalisability of the paired *t*-test because participants with missing paired values have to be excluded from the analyses.

Assumptions for a paired *t*-test

Independent two-sample *t*-tests cannot be used for analysing paired or matched data because the assumption that the two groups are independent, that is data are collected from different or non-matched participants, would be violated. Treating paired or matched measurements as independent samples will artificially inflate the sample size and lead to inaccurate analyses.

The assumptions for using paired *t*-tests are shown in Box 4.1.

Box 4.1 Assumptions for a paired *t*-test

For a paired *t*-test the following assumptions must be met:

- the outcome variable has a continuous scale
- the differences between the pairs of measurements are normally distributed

The data file **growth.sav** contains the body measurements of 277 babies measured at 1 month and at 3 months of age.

Questions: Does the weight of babies increase significantly in a 2-month growth period?
Does the length of babies increase significantly in a 2-month growth period?
Does the head circumference of babies increase significantly in a 2-month growth period?

Null hypotheses: The weight of babies is not different between the two time periods.
The length of babies is not different between the two time periods.
The head circumference of babies is not different between the two time periods.

Variables: Outcome variables = weight, length and head circumference measured at 1 month of age and 3 months of age (continuous)

The decision of whether to use a one- or two-tailed test must be made when the study is designed. If a one-tailed *t*-test is used, the null hypothesis is more likely to be rejected than if a two-tailed test is used (Chapter 3). In general, two-tailed tests should always be used unless there is a good reason for not doing so and a one-tailed test should only be used when the direction of effect is specified in advance[2]. In this example, it makes sense to test for a significant increase in body measurements because there is certainty that a decrease will not occur and there is only one biologically plausible direction of effect. Therefore a one-tailed test is appropriate for the alternate hypothesis.

To test the assumption that the differences between the two outcome variables is normally distributed, the differences between measurements taken at 1 month and at 3 months must first be computed as shown in Box 4.2.

Box 4.2 SPSS commands to transform variables

SPSS Commands

growth – SPSS Data Editor
    Transform → Compute
Compute Variable
    Target Variable = diffwt
    Numeric Expression = Weight at 3mo – Weight at 1mo
    Click OK

By clicking on the *Reset* button in *Compute Variable* all fields will be reset to empty and the command sequence shown in Box 4.2 can be used to compute the following variables:

diffleng = Length at 3mo − Length at 1mo, *and*

diffhead = Head circumference at 3mo − Head circumference at 1mo

Once the new variables are created, they should be labelled and have the number of decimal places adjusted to be appropriate. The distribution of these differences between the paired measurements can then be examined using the commands shown in Box 4.3 to obtain histograms. While only histograms have been obtained in this example, in practice a thorough investigation of all tests of normality should be undertaken using *Analyze → Descriptive Statistics → Explore* and other options discussed in Chapter 2.

Box 4.3 SPSS commands to obtain frequency histograms

SPSS Commands

    Graphs → Histogram
Histogram
    Variable = Weight 3mo-1mo
    Tick box 'Display normal curve'
    Click OK

The command sequence in Box 4.3 can then be repeated with the variables Length 3m-1mo and Head 3mo-1mo to produce the histograms shown in Figure 4.1. The histograms indicate that all three difference variables are fairly normally distributed with only a slight skew to the right hand side. A paired *t*-test will be robust to these small departures from normality because with 277 babies the sample size is large.

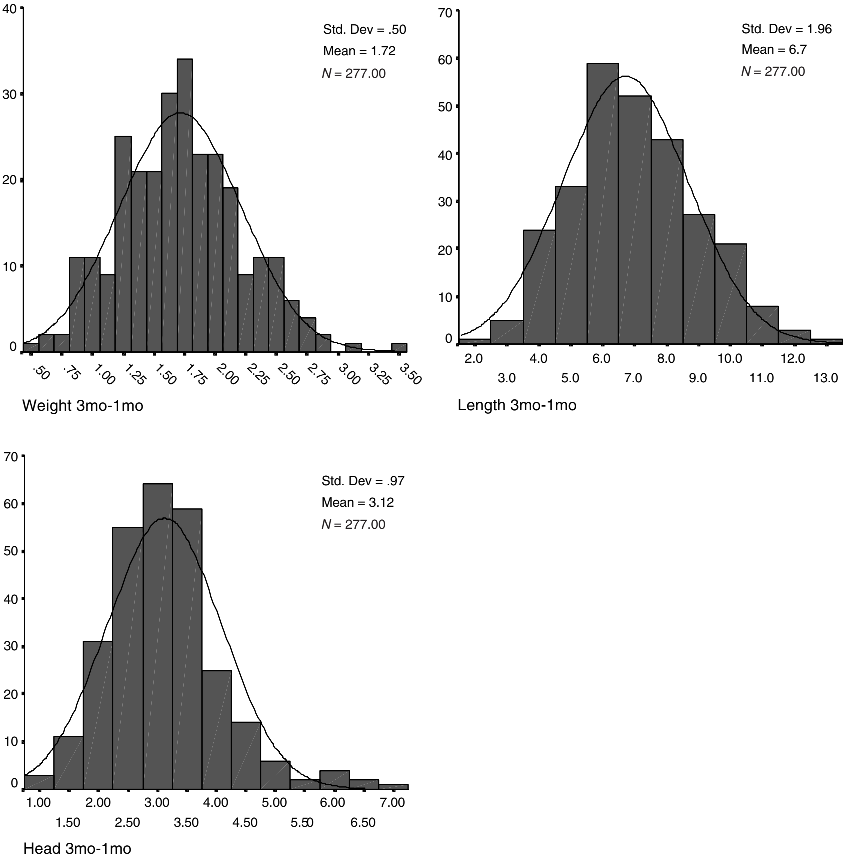

Figure 4.1 Histograms of differences between babies at 1 month and 3 months for weight, length and head circumference.

The SPSS commands to conduct a paired samples *t*-test to examine whether there has been a significant increase in weight, length and head circumference are shown in Box 4.4. By holding down the Ctrl key, two variables can be highlighted and clicked over simultaneously into the Paired Variables box.

Box 4.4 SPSS commands to obtain a paired samples t-test

SPSS Commands

growth – SPSS Data Editor
Analyze → Compare Means → Paired-Samples T Test
Paired-Samples T-Test
Highlight Weight at 1mo (Variable 1) and Weight at 3mo (Variable 2) and click over into the Paired Variables box (weight1m – weight3m)
Highlight Length at 1mo (Variable 1) and Length at 3mo (Variable 2) and click over into the Paired Variables box (length1m – length3m)
Highlight Head circumference at 1m (Variable 1) and Head circumference at 3mo (Variable 2) and click over into the Paired Variables box (head1m – head3m)
Click OK

t-test

Paired Samples Statistics

		Mean	***N***	**Std. deviation**	**Std. error mean**
Pair 1	Weight at 1 mo (kg)	4.415	277	0.6145	0.0369
	Weight at 3 mo (kg)	6.131	277	0.7741	0.0465
Pair 2	Length at 1 mo (cm)	54.799	277	2.3081	0.1387
	Length at 3 mo (cm)	61.510	277	2.7005	0.1623
Pair 3	Head circumference at 1 mo (cm)	37.918	277	1.3685	0.0822
	Head circumference at 3 mo (cm)	41.039	277	1.3504	0.0811

Paired Samples Correlations

		N	**Correlation**	**Sig.**
Pair 1	Weight at 1 mo (kg) & Weight at 3 mo (kg)	277	0.768	0.000
Pair 2	Length at 1 mo (cm) & Length at 3 mo (cm)	277	0.703	0.000
Pair 3	Head circumference at 1 mo (cm) & Head circumference at 3 mo (cm)	277	0.746	0.000

The Paired Samples Statistics table provides summary statistics for each variable but does not give any information that is relevant to the paired t-test. The

Paired Samples Correlations table shows the correlations between each of the paired measurements. This table should be ignored because it does not make sense to test the hypothesis that two related measurements are associated with one another.

Paired Samples Test

		Paired differences							
					95% confidence interval of the difference				
		Mean	Std. deviation	Std. error Mean	Lower	Upper	*t*	df	Sig. (Two-tailed)
Pair 1	Weight at 1 mo (kg) – weight at 3 mo (kg)	−1.717	0.4961	0.0298	−1.775	−1.658	−57.591	276	0.000
Pair 2	Length at 1mo (cm) – length at 3 mo (cm)	−6.710	1.9635	0.1180	−6.943	−6.478	−56.881	276	0.000
Pair 3	Head circumference at 1 mo (cm) – head circumference at 3 mo (cm)	−3.121	0.9697	0.0583	−3.236	−3.006	−53.565	276	0.000

The Paired Samples Test table provides important information about the *t*-test results. The second column, which is labelled Mean, gives the main outcome statistic, that is the mean within-pair difference. When conducting a paired *t*-test, the means of the differences between the pairs of variables are computed as part of the test. The only way to control the direction of the mean differences is by organising the order of variables in the spreadsheet. In the data set, weight at 1 month occurs before weight at 3 months, so it is not possible to obtain a paired samples *t*-test with weight at 3mo as Variable 1 and weight at 1mo as Variable 2 unless the data set is re-organised.

The mean paired differences column in the table indicates that at 1 month, babies were on average 1.717 kg lower in weight, 6.71 cm smaller in length and 3.121 cm smaller in head circumference than at 3 months of age. These mean values do not answer the research question of whether babies increased significantly in measurements over a 2-month period but rather answer the question of whether the babies were smaller at a younger age.

The 95% confidence intervals of the differences, which are calculated as the mean paired differences ± (1.96 * SE of mean paired differences), do not contain the value of zero for any variable which also indicates that the difference in body size between 1 and 3 months is statistically significant. The *t* value is calculated as the mean differences divided by their standard error. Because the standard error becomes smaller as the sample size becomes larger, the *t* value increases as the sample size increases for the same mean difference. Thus, in this example with a large sample size of 277 babies, relatively small mean differences are highly statistically significant.

The *P* values provided in the Paired Samples Test table are for a two-tailed test, so they have to be adjusted for a one-sample test by halving the *P* value. In this example, the *P* values are <0.0001 so that halving them will also render a highly significant P value. The P values (one tailed) from the paired t-tests for all three variables indicate that each null hypothesis should be rejected and that there is a significant increase in body measurements between the two time periods. By multiplying the mean difference values by −1, to obtain the mean difference in the correct direction (i.e. weight at 3 months − weight at 1 month), babies over a 2-month period were significantly heavier (+1.72 kg, $P < 0.0001$), longer (+6.71 cm, $P < 0.0001$) and had a larger head circumference (+3.12 cm, $P < 0.0001$). As with any statistical test, it is important to decide whether the size of mean difference between measurements would be considered clinically important in addition to considering statistical significance.

Non-parametric test for paired data

A non-parametric equivalent of the paired t-test is the Wilcoxon signed rank test, which is also called the Wilcoxon matched pairs test and is used when lack of normality in the differences is a concern or when the sample size is small. The Wilcoxon signed rank test is used to test whether the median of the differences is equal to zero.

An assumption of the Wilcoxon signed rank test is that the paired differences are independent and come from the same continuous and symmetric population distribution. This test is relatively resistant to outliers. However, the number of outliers should not be large relative to the sample size and the amount of skewness should be equal in both groups. When the sample size is small, symmetry may be difficult to assess.

In this test, the absolute differences between paired scores are ranked and difference scores that are equal to zero, that is indicate no difference between pairs, are excluded from the analysis. Thus, this test is not suitable when a large proportion of paired differences are equal to zero because this effectively reduces the sample size.

If the difference values in the **growth.sav** data set did not have a normal distribution, the Wilcoxon signed rank test could be obtained using the SPSS commands in Box 4.5.

Box 4.5 SPSS commands to conduct a non-parametric paired test

SPSS Commands

growth – SPSS Data Editor

Analyze → Nonparametric Tests → 2 Related Samples

Two Related Samples

Click on Weight at 1mo (Variable 1) and click on Weight at 3mo (Variable 2)

Click on the arrow to place variables under Test Pair(s) List (weight1m – weight3m)

Click on Length at 1mo (Variable 1) and click on Length at 3mo (Variable 2)

Click on the arrow to place variables under Test Pair(s) List (length1m – length3m)
Click on Head circumference at 1mo (Variable 1) and click on Head circumference at 3mo (Variable 2)
Click on the arrow to place variables under Test Pair(s) List (head1m – head3m)
Test Type = tick Wilcoxon (default setting)
Click Options
Two-Related-Samples: Options
Tick Quartiles
Click Continue
Two Related Samples
Click OK

NPar tests

Descriptive Statistics

		Percentiles		
	N	**25th**	**50th (median)**	**75th**
Weight at 1 mo (kg)	277	4.000	4.350	4.815
Length at 1 mo (cm)	277	53.000	54.500	56.500
Head circumference at 1 mo (cm)	277	37.000	38.000	39.000
Weight at 3 mo (kg)	277	5.550	6.040	6.680
Length at 3 mo (cm)	277	59.500	61.500	63.500
Head circumference at 3 mo (cm)	277	40.000	41.000	42.000

Instead of providing information about mean values, this non-parametric test provides the median and the 25th and 75th percentile values as summary statistics. These are the summary statistics that would be used in box plots or reported in tables of results.

Wilcoxon Signed Rank Test

Ranks

		N	**Mean Rank**	**Sum of Ranks**
Weight at 3 mo (kg) – weight at 1 mo (kg)	Negative ranks	0[a]	0.00	0.00
	Positive ranks	277[b]	139.00	38503.00
	Ties	0[c]		
	Total	277		

Continued

Ranks *continued*

		N	Mean Rank	Sum of Ranks
Length at 3 mo (cm) − length at 1 mo (cm)	Negative ranks	0[d]	0.00	0.00
	Positive ranks	277[e]	139.00	38503.00
	Ties	0[f]		
	Total	277		
Head circumference at 3 mo (cm) − Head circumference at 1 mo (cm)	Negative ranks	0[g]	0.00	0.00
	Positive ranks	277[h]	139.00	38503.00
	Ties	0[i]		
	Total	277		

[a] Weight at 3 months (kg) < Weight at 1 month (kg)
[b] Weight at 3 months (kg) > Weight at 1 month (kg)
[c] Weight at 1 month (kg) = Weight at 3 months (kg)
[d] Length at 3 months (cm) < Length at 1 month (cm)
[e] Length at 3 months (cm) > Length at 1 month (cm)
[f] Length at 1 month (cm) = Length at 3 months (cm)
[g] Head circumference at 3 months (cm) < Head circumference at 1 month (cm)
[h] Head circumference at 3 months (cm) > Head circumference at 1 month (cm)
[i] Head circumference at 1 month (cm) = Head circumference at 3 months (cm)

Test Statistics[b]

	Weight at 3 months (kg) − weight at 1 month (kg)	**Length at 3 months (cm) − length at 1 month (cm)**	**Head circumference at 3 months (cm) − head circumference at 1 month (cm)**
Z	−14.427[a]	−14.438[a]	−14.470[a]
Asymp. sig. (two-tailed)	0.000	0.000	0.000

[a] Based on negative ranks.
[b] Wilcoxon signed ranks test.

The *P* values that are computed are based on the ranks of the absolute values of the differences between time 1 (1 month) and time 2 (3 months). The number of negative ranks where time 1 is lower than time 2 is compared to the number of positive ranks where time 1 is higher than time 2 with the zero ranks omitted. In this test the summary statistics are given the opposite direction of effect to the paired *t*-test and, in this case, give the correct direction of effect.

The Ranks table indicates that, as expected, no babies have a negative rank that is a lower measurement at 1 month than at 3 months. The table also shows that there are no ties, that is no babies with the same difference scores. Although this table does not provide any useful information for communicating the size of effect, it does indicate the correct direction of effect. The test statistics with a P value of <0.0001 for all variables show that there has been a significant increase in all measurements from 1 month (baseline) to 3 months. Because the data are fairly normally distributed, both the parametric test and the non-parametric test give the same P values.

The results of this non-parametric test would be reported as for a paired t-test except that the median differences rather than the mean differences would be reported and, if required, the inter-quartile range and the z score would be reported rather than the standard deviation and the paired t value.

Standardising for differences in baseline measurements

With paired data, the differences between the pairs are sometimes not an appropriate outcome of interest. It is often important that the differences are standardised for between-subject differences in baseline values. One method is to compute a per cent change from baseline. Another method is to calculate the ratio between the follow-up and baseline measurements. It is important to choose a method that is appropriate for the type of data collected and that is easily communicated.

For babies' growth, per cent change is a simple method to standardise for differences in body size at baseline, that is at 1 month of age. The syntax shown in Box 4.6 can be used to compute per cent growth in weight, length and head circumference.

Box 4.6 SPSS commands to compute per cent changes

SPSS Commands

```
growth – SPSS Data Editor
        Transform → Compute
Compute Variable
        Target Variable = perwt
        Numeric Expression = (Weight at 3mo – Weight at 1mo) * 100/
            Weight at 1mo
        Click Paste
Syntax1 – SPSS Syntax Editor
        Run → All
```

The syntax can then be repeated to compute:

Perleng = (*Length at 3mo - Length at 1mo*)*100/*Length at 1mo, and*

Perhead = (*Head circumference at 3mo - Head circumference at 1mo*)*100/
Head circumference at 1mo

The paste and run commands list the transformations in the syntax window as shown below. This information can then be printed and stored for documentation. Once the computations are complete, the new variables need to be labelled in the Variable View window.

```
COMPUTE perwt = (weight3m – weight1m)*100/weight1m.
EXECUTE.
COMPUTE perlen = (length3m – length1m)*100/length1m.
EXECUTE.
COMPUTE perhead = (head3m – head1m)*100/head1m.
EXECUTE.
```

An assumption of paired *t*-tests is that the differences between the pairs of measurements are normally distributed, therefore the distributions of the per cent changes need to be examined. Again, the distributions should be fully checked for normality using *Analyze → Descriptive Statistics → Explore* as discussed in Chapter 2. The histograms shown in Figure 4.2 can be obtained

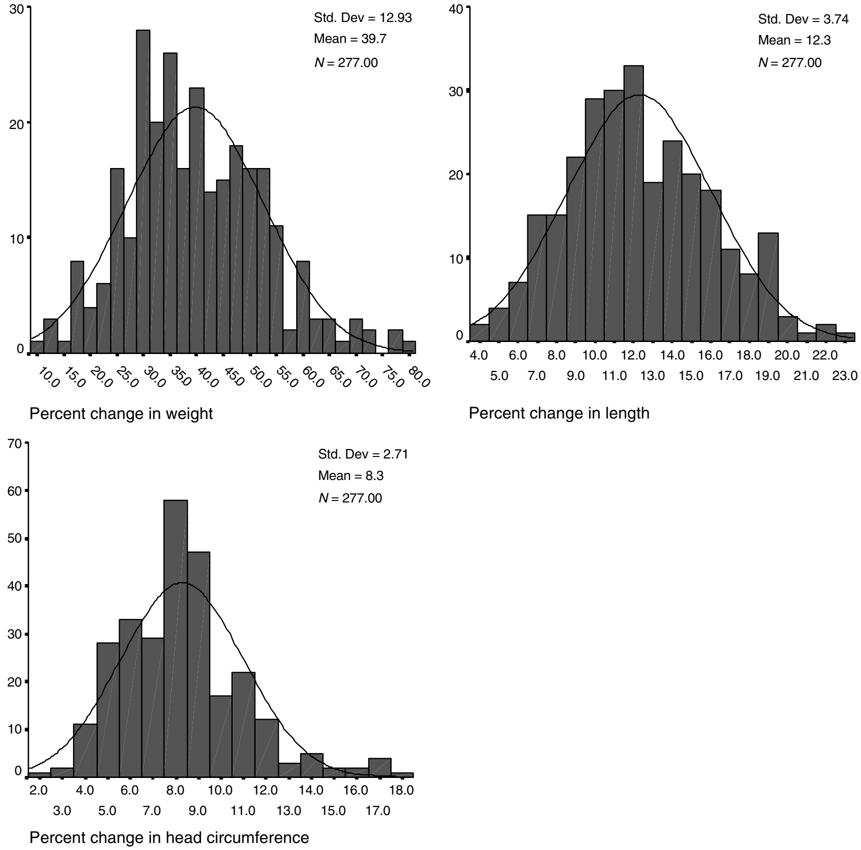

Figure 4.2 Histograms of per cent change in weight, length and head circumference.

using the commands shown in Box 4.3. The histograms for per cent change in weight and head circumference have a small tail to the right, but the sample size is large and the tails are not so marked that the assumptions for using a paired *t*-test would be violated.

Single-sample *t*-test

The research question has now changed slightly because rather than considering absolute differences between time points, the null hypothesis being tested is whether the mean per cent changes over time are significantly different from zero. With differences converted to a per cent change, there is now a single continuous outcome variable and no group variable. Thus, a one-sample *t*-test, which is also called a single-sample *t*-test, can be used to test whether there is a statistically significant difference between the mean per cent change and a fixed value such as zero.

A one-sample test is more flexible than a paired *t*-test, which is limited to testing whether the mean difference is significantly different from zero. One-sample *t*-tests can be used, for example, to test if the sample has a different mean from 100 points if the outcome being measured is IQ or from 40 hours if the outcome measured is the average working week. A one-sample *t*-test is a parametric test and the only assumption is that the data, in this case per cent increases, are normally distributed.

Computing per cent changes provides control over the units that the changes are expressed in and their direction of effect. However, if the differences computed in Box 4.2 were used as the outcome and a one-sample *t*-test was used to test for a difference from zero, the one-sample *t*-test would give exactly the same *P* values as the paired *t*-test although the direction of effect would be correctly reversed.

For the research question, the command sequence shown in Box 4.7 can be used to compute a one-sample *t*-test to test whether the per cent changes in weight, length and head circumference are significantly different from zero.

Box 4.7 SPSS commands to conduct a one-sample *t*-test

SPSS Commands

Growth – SPSS Data Editor

Analyze → Compare Means → One-Sample T Test

One-Sample T Test

Highlight the variables Percent change in weight, Percent change in length and Percent change in head circumference and click into the Test Variable(s) box

Test Value = 0 (default setting)

Click OK

t-test

One-Sample Statistics

	N	Mean	Std. deviation	Std. error mean
Per cent change in weight	277	39.7264	12.9322	0.7770
Per cent change in length	277	12.2980	3.7413	0.2248
Per cent change in head circumference	277	8.2767	2.7115	0.1629

The One-Sample Statistics table gives more relevant statistics with which to answer the research question because the mean within-participant per cent changes and their standard deviations are provided. The means in this table show that the per cent increase in weight over 2 months is larger than the per cent increase in length and head circumference.

One-Sample Test

	Test value = 0					
					95% confidence interval of the difference	
	t	*df*	Sig. (two-tailed)	Mean difference	Lower	Upper
Per cent change in weight	51.126	276	0.000	39.7264	38.1968	41.2561
Per cent change in length	54.708	276	0.000	12.2980	11.8555	12.7406
Per cent change in head circumference	50.803	276	0.000	8.2767	7.9559	8.5974

In the One-Sample Test table, the t values are again computed as mean difference divided by the standard error and, in this table, are highly significant for all measurements. The highly significant P values are reflected in the 95% confidence intervals, none of which contain the zero value. The outcomes are now all in the same units, that is per cent change, and therefore growth rates between the three variables can be directly compared. This was not possible before when the variables were in their original units of measurement. This summary information could be reported as shown in Table 4.1. In some disciplines, the t value is also reported with its degrees of freedom, for example as t (276) = 51.13 but because the only interpretation of the t value and its degrees of freedom is the P value, it is often excluded from summary tables.

Table 4.1 Mean body measurements and per cent change between 1 and 3 months in 277 babies

	1 month Mean (SD)	3 months Mean (SD)	Per cent increase and 95% CI	*P* value
Weight (kg)	4.42 (0.62)	6.13 (0.77)	39.7 (38.2, 41.3)	<0.0001
Length (cm)	54.8 (2.3)	61.5 (2.7)	12.3 (11.9, 12.7)	<0.0001
Head circumference (cm)	37.9 (1.4)	41.0 (1.4)	8.3 (7.9, 8.6)	<0.0001

Research question

The research question can now be extended to ask if certain groups, such as males and females, have different patterns or rates of growth.

Questions: Over a 2-month period:
- do males increase in weight significantly more than females?
- do males increase in length significantly more than females?
- do males increase in head circumference significantly more than females?

Null hypothesis: Over a 2-month period:
- there is no difference between males and females in weight growth.
- there is no difference between males and females in length growth.
- there is no difference between males and females in head circumference growth.

Variables: Outcome variables = per cent increase in length, weight and head circumference (continuous)
Explanatory variable = gender (categorical, binary)

The research question then becomes a two-sample *t*-test again because there is a continuously distributed variable (per cent change) and a binary group variable with two levels that are independent (male, female). The SPSS commands shown in Box 3.3 in Chapter 3 can be used to obtain the following output.

t-test

Group Statistics

	Gender	*N*	Mean	Std. deviation	Std. error mean
Per cent change in weight	Male	148	42.0051	13.2656	1.0904
	Female	129	37.1121	12.0676	1.0625

Continued

Group Statistics *continued*

	Gender	*N*	Mean	Std. deviation	Std. error mean
Per cent change in length	Male	148	12.6818	3.3079	0.2719
	Female	129	11.8577	4.1533	0.3657
Per cent change in head circumference	Male	148	8.2435	2.5066	0.2060
	Female	129	8.3147	2.9385	0.2587

The means in the Group Statistics table show that males have a higher increase in weight and length than females but a slightly lower increase in head circumference. These statistics are useful for summarising the magnitude of the differences in each gender.

In the Independent Samples Test table (opposite), Levene's test of equality of variances shows that the variances are not significantly different between genders for weight ($P = 0.374$) and head circumference ($P = 0.111$). For these two variables, the *Equal variances assumed* rows in the table are used. However, the variance in per cent change for length is significantly different between the genders ($P = 0.034$) and therefore the appropriate t value, degrees of freedom and P value for this variable are shown in the *Equal variances not assumed* row. An indication that the variances are unequal could be seen in the previous Group Statistics table, which shows that the standard deviation for per cent change in length is 3.3079 for males and 4.1533 for females. An estimate of the variances can be obtained by squaring the standard deviations to give 10.94 for males and 17.25 for females, which is a variance ratio of 1:1.6.

Thus, the Independent Samples Test table shows that per cent increase in weight is significantly different between the genders at $P = 0.002$, per cent increase in length does not reach significance between the genders at $P = 0.072$ and per cent increase in head circumference is not clearly not different between the genders at $P = 0.828$. This is reflected in the 95% confidence intervals, which do not cross zero for weight, cross zero marginally for length and encompass zero for head circumference.

Presenting the results

The growth patterns for weight are different between genders and therefore it is important to present the one-sample t-test results for each gender separately. If no between-gender differences were found, the summary statistics for the entire sample could be presented. In this case, one-sample t-tests are used to test whether the mean per cent increase is significantly different from zero for each gender. This can be achieved using the *Split File* option shown in Box 4.8. After the commands have been completed, the message *Split File On* will appear in the bottom right hand side of the Data Editor screen. The advantage of using *Split File* rather than *Select Cases* is that the output will be automatically documented with group status.

Independent Samples Test

				t-test for equality of means						
		Levene's test for equality of variances							95% confidence interval of the difference	
		F	Sig.	*t*	*df*	Sig. (Two-tailed)	Mean difference	Std. error difference	Lower	Upper
Per cent change in weight	Equal variances assumed	0.792	0.374	3.193	275	0.002	4.8930	1.53240	1.87633	7.90976
	Equal variances not assumed			3.214	274.486	0.001	4.8930	1.52247	1.89583	7.89025
¶ Per cent change in length	Equal variances assumed	4.518	0.034	1.837	275	0.067	0.8241	0.44873	−0.05928	1.70748
	Equal variances not assumed			1.808	243.779	0.072	0.8241	0.45569	−0.07350	1.72170
¶ Per cent change in head circumference	Equal variances assumed	2.561	0.111	−0.217	275	0.828	−0.0711	0.32717	−0.71521	0.57294
	Equal variances not assumed			−0.215	253.173	0.830	−0.0711	0.33074	−0.72248	0.58021

Box 4.8 SPSS commands to compare gender means

SPSS Commands

growth – SPSS Data Editor
    Data → Split File
Split File
    Click Compare groups
    Highlight Gender and click over into 'Groups Based on'
    Click OK

The one-sample *t*-test for each gender can then be obtained using the commands shown in Box 4.7 to produce the following output.

t-test

One-Sample Statistics

Gender		***N***	**Mean**	**Std. deviation**	**Std. error mean**
Male	Per cent change in weight	148	42.0051	13.2656	1.0904
	Per cent change in length	148	12.6818	3.3079	0.2719
	Per cent change in head circumference	148	8.2435	2.5066	0.2060
Female	Per cent change in weight	129	37.1121	12.0676	1.0625
	Per cent change in length	129	11.8577	4.1533	0.3657
	Per cent change in head circumference	129	8.3147	2.9385	0.2587

One-Sample Test

		Test value = 0					
						95% confidence interval of the difference	
Gender		***t***	***df***	**Sig. (Two-tailed)**	**Mean difference**	**Lower**	**Upper**
Male	Per cent change in weight	38.522	147	0.000	42.0051	39.8502	44.1601
	Per cent change in length	46.640	147	0.000	12.6818	12.1445	13.2192
	Per cent change in head circumference	40.010	147	0.000	8.2435	7.8363	8.6507

Continued

		Test value = 0					
						95% confidence interval of the difference	
Gender		***t***	***df***	**Sig. (Two-tailed)**	**Mean difference**	**Lower**	**Upper**
Female	Per cent change in weight	34.929	128	0.000	37.1121	35.0098	39.2144
	Per cent change in length	32.426	128	0.000	11.8577	11.1342	12.5813
	Per cent change in head circumference	32.138	128	0.000	8.3147	7.8027	8.8266

The One-Sample Statistics table gives the same summary statistics as obtained in the two-sample *t*-test but gives a *P* value for the significance of the per cent change from baseline for each gender and also gives the 95% confidence intervals around the mean changes. Another alternative to obtaining summary means for each gender is to use the commands shown in Box 4.9, but with the *Split File* option removed.

Box 4.9 SPSS commands to obtain summary mean values

SPSS Commands

growth – SPSS Data Editor

Data → Split File

Split File

Click Analyze all cases, do not create groups

Click OK

growth – SPSS Data Editor

Analyze → Compare Means → Means

Means

Click variables for weight, length, head circumference at 1 month (weight1m, length1m, head1m) and at 3 months (weight3m, length3m, head3m) and all three percent changes (perwt, perlen, perhead) into the Dependent List box

Click Gender over into the Independent List box

Click OK

Means

Report

Gender		Weight at 1 mo (kg)	Length at 1 mo (cm)	Head circumference at 1 mo (cm)	Weight at 3 mo (kg)	Length at 3 mo (cm)	Head circumference at 3 mo (cm)	Per cent change in weight	Per cent change in length	Per cent change in head circumference
Male	Mean	4.534	55.249	38.259	6.389	62.218	41.393	42.0051	12.6818	8.2435
	N	148	148	148	148	148	148	148	148	148
	Std. deviation	0.6608	2.5636	1.3252	0.7829	2.6185	1.1411	13.26558	3.30790	2.50656
Female	Mean	4.278	54.283	37.526	5.836	60.698	40.632	37.1121	11.8577	8.3147
	N	129	129	129	129	129	129	129	129	129
	Std. deviation	0.5269	1.8539	1.3160	0.6507	2.5704	1.4575	12.06764	4.15334	2.93850
Total	Mean	4.415	54.799	37.918	6.131	61.510	41.039	39.7264	12.2980	8.2767
	N	277	277	277	277	277	277	277	277	277
	Std. deviation	0.6145	2.3081	1.3685	0.7741	2.7005	1.3504	12.93223	3.74134	2.71147

The Report table completes the information needed to report the results as shown in Table 4.2. Although a one-tailed *P* value is used for the significance of increases in body size, a two-tailed *P* value is used for between-gender comparisons.

Table 4.2 Mean body measurements and per cent change between 1 and 3 months in 148 male and 129 female babies

		1 month Mean (SD)	3 months Mean (SD)	Per cent change and 95% CI	*P* value for change from baseline	*P* value for difference between genders
Weight (kg)	Male	4.53 (0.66)	6.39 (0.78)	42.0 (39.9, 44.2)	<0.0001	0.002
	Female	4.28 (0.53)	5.84 (0.65)	37.1 (35.0, 39.2)	<0.0001	
Length (cm)	Male	55.2 (2.6)	62.2 (2.6)	12.7 (12.1, 13.2)	<0.0001	0.072
	Female	54.3 (1.9)	60.7 (2.6)	11.9 (11.1, 12.6)	<0.0001	
Head circumference (cm)	Male	38.3 (1.3)	41.4 (1.1)	8.2 (7.8, 8.7)	<0.0001	0.828
	Female	37.5 (1.3)	40.6 (1.5)	8.3 (7.8, 8.8)	<0.0001	

When plotting summary statistics of continuous variables, the choice of whether to use bar charts or dot points is critical. Bar charts should always begin at zero so that their lengths can be meaningfully compared. When the distance from zero has no meaning, mean values are best plotted as dot points. For example, mean length would not be plotted using a bar chart because no baby has a zero length. However, bar charts are ideal for plotting per cent changes where a zero value is plausible. The results can be plotted as bar charts in SigmaPlot by entering the data as follows and using the commands shown in Box 4.10. The means for males are entered in column 1 and the 95% confidence interval width in column 2. The values for females are entered in columns 3 and 4. The column titles should not be entered in the spreadsheet cells.

Column 1	Column 2	Column 3	Column 4
42.0	2.1	37.1	2.1
12.7	0.6	11.9	0.6
8.2	0.4	8.3	0.4

Box 4.10 SigmaPlot commands for graphing per cent change results

SigmaPlot Commands

SigmaPlot – [Data 1]

Graph → Create Graph

Create Graph – Type
Highlight Horizontal Bar Chart, click Next
Create Graph –Style
Highlight Grouped Error Bars, click Next
Create Graph – Error Bars
Symbol Values = Worksheet Columns (default), click Next
Create Graph – Data Format
Highlight Many X, click Next
Create Graph – Select Data
Data for Set 1 = use drop box and select Column 1
Data for Error 1 = use drop box and select Column 2
Data for Set 2 = use drop box and select Column 3
Data for Error 2 = use drop box and select Column 4
Click Finish

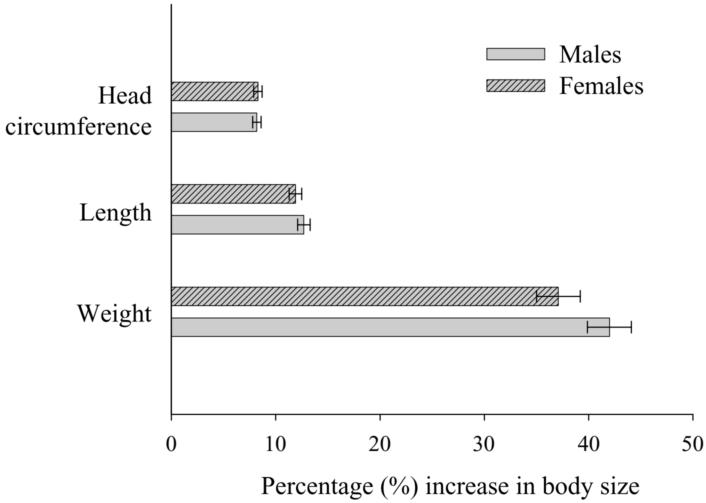

Figure 4.3 Per cent increase in growth from age 1 to 3 months.

The plot can then be customised by changing the axes, fills, labels etc in *Graph* → *Graph Properties* menus.

Notes for critical appraisal

Questions to ask when assessing statistics from paired or matched data are shown in Box 4.11.

Box 4.11 Questions for critical appraisal

The following questions should be asked when appraising published results from paired or matched data:

- Has an appropriate paired *t*-test or single sample test been used?
- Do the within-pair differences need to be standardised for baseline differences, that is presented as per cent changes or ratios?
- Are the within-pair differences normally distributed?
- If summary statistics are reported, are they in the same units of change so that they can be directly compared if necessary?
- Have rank based non-parametric tests been used for non-normally distributed differences?
- Have descriptive data been reported for each of the pair of variables in addition to information of mean changes?

References

1. Bland JM, Altman DG. Matching. BMJ 1994; 309: 1128.
2. Bland JM, Altman DG. One and two sided tests of significance. BMJ 1994; 309: 248.

CHAPTER 5
Continuous variables: analysis of variance

I discovered, though unconsciously and insensibly, that the pleasure of observing and reasoning was a much higher one that that of skill and sports.
CHARLES DARWIN.

Objectives

The objectives of this chapter are to explain how to:

- decide when to use an ANOVA test
- run and interpret the output from a one-way or a factorial ANOVA
- understand between-group and within-group differences
- classify factors into fixed, interactive or random effects
- test for a trend across the groups within a factor
- perform post-hoc tests
- build a multivariate ANCOVA model
- report the findings from an ANOVA model
- test the ANOVA assumptions

A two-sample *t*-test can only be used to assess the significance of the difference between the mean values of two independent groups. To compare differences in the mean values of three or more independent groups, analysis of variance (ANOVA) is used. Thus, ANOVA is suitable when the outcome measurement is a continuous variable and when the explanatory variable is categorical with three or more groups. An ANOVA model can also be used for comparing the effects of several categorical explanatory variables at one time or for comparing differences in the mean values of one or more groups after adjusting for a continuous variable, that is a covariate.

A one-way ANOVA is used when the effect of only one categorical variable (explanatory variable) on a single continuous variable (outcome) is explored, for example when the effect of socioeconomic status, which has three groups (low, medium and high), on weight is examined. The concept of ANOVA can be thought of as an extension of a two-sample *t*-test but the terminology used is quite different. A factorial ANOVA is used when the effects of two or more categorical variables (explanatory variables) on a single continuous variable (outcome) are explored, for example when the effects of gender and socioeconomic status on weight are examined.

An analysis of covariance (ANCOVA) is used when the effects of one or more categorical factors (explanatory variables) on a single continuous variable (outcome) are explored after adjusting for the effects of one or more continuous variables (covariates). A covariate is any variable that correlates with the outcome variable. For example, ANCOVA would be used to test for the effects of gender and socioeconomic status on weight after adjusting for height.

For both ANOVA and ANCOVA, the theory behind the model must be reliable in that there must be biological plausibility or scientific reason for the effects of the factors being tested. In this, it is important that the factors are independent and not related to one another. For example, it would not make sense to test for differences in mean values of an outcome between groups defined according to education and socioeconomic status when these two variables are related. Once the results of an analysis of variance are obtained, they can only be generalised to the population if the data were collected from a random sample, and a significant *P* value cannot be taken as evidence of causality.

Building an ANOVA model

When building an ANOVA or ANCOVA model, it is important to build the model in a logical and considered way. The process of model building is as much an art as a science. Descriptive and summary statistics should always be obtained first to provide a good working knowledge of the data before beginning the bivariate analyses or multivariate modelling. In this way, the model can be built up in a systematic way, which is preferable to including all variables in the model and then deciding which variables to remove from the model, that is, using a backward elimination process. Table 5.1 shows the steps in the model building process.

Table 5.1 Steps in building an ANOVA model

Type of analysis	SPSS procedure	Purpose
Univariate analyses	Explore	Examine cell sizes Obtain univariate means Test for normality
Bivariate analyses	Crosstabulations One-way ANOVA	Ensure adequate cell sizes Estimate differences in means and homogeneity of variances Examine trends across groups within a factor
Multivariate analyses	Factorial ANOVA ANCOVA	Test several explanatory factors or adjust for covariates Test normality of residuals Test influence of multivariate outliers

Assumptions for ANOVA models

The assumptions for ANOVA, which must be met in all types of ANOVA models, are shown in Box 5.1.

Box 5.1 Assumptions for using ANOVA

The assumptions that must be met when using one-way or factorial ANOVA are as follows:

- the participants must be independent, that is each participant appears only once in their group
- the groups must be independent, that is each participant must be in one group only
- the outcome variable is normally distributed
- all cells have an adequate sample size
- the cell size ratio is no larger than 1:4
- the variances are similar between groups
- the residuals are normally distributed
- there are no influential outliers

The first two assumptions are similar to the assumptions for two-sample *t*-tests and any violation will invalidate the analysis. In practice, this means that each participant should appear on one data row of the spreadsheet only and thus will be included in the analysis once only. When cases appear in the spreadsheet on more than one occasion then repeated ANOVA should be used in which case the ID numbers are included as a factor.

When an ANOVA is conducted, the data are divided into cells according to the number of groups in the explanatory variable. Small cell sizes, that is cell sizes less than 10, are always problematic because of the lack of precision in calculating the mean value for the cell. The minimum cell size in theory is 10 but in practice 30 is preferred. In addition to creating imprecision, low cell counts lead to a loss of statistical power. The assumption of a low cell size ratio is also important. A cell size imbalance of more than 1:4 across the model would be a concern, for example when one cell has 10 cases and another cell has 60 cases and the ratio is then 1:6.

It may be difficult to avoid small cell sizes because it is not possible to predict the number of cases in each cell prior to data collection. Even in experimental studies in which equal numbers can be achieved in some groups, drop-outs and missing data can lead to unequal cell sizes. If small cells are present, they can be re-coded into larger cells but only if it is possible to meaningfully interpret the re-coding.

Both the assumptions of a normal distribution and equality of the variance of the outcome variable between cells should be tested before ANOVA is conducted. However, as with a *t*-test, ANOVA is robust to some deviations from normality of distributions and some imbalance of variances. The assumption that the outcome variable is normally distributed is of most importance when the sample size is small and/or when univariate outliers increase or decrease mean values between cells by an important amount and therefore influence perceived differences between groups. The main effects of non-normality and unequal variances, especially if there are outliers, are to bias the *P* values. However, the direction of the bias may not be clear.

When variances are not significantly different between cells, the model is said to be homoscedastic. The assumption of equal variances is of most importance when there are small cells, say cells with less than 30 cases, when the cell size ratio is larger than 1:4 or when there are large differences in variance between cells, say larger than 1:10. The main effect of unequal variance is to reduce statistical power and thus lead to type II errors. Equality of variances should be tested in bivariate analyses before running an ANOVA model and then re-affirmed in the final model.

One-way ANOVA

A one-way ANOVA test is very similar to a two-sample *t*-test but in ANOVA the explanatory variable, which is called a factor, has more than two groups. For example, a factor could be participants' residential area with three groups: inner city, outer suburbs and rural. A one-way ANOVA is used to test the null hypothesis that each group within the factor has the same mean value.

The ANOVA test is called an analysis of variance and not an analysis of means because this test is used to assess whether the mean values of different groups are far enough apart in terms of their spread (variance) to be considered significantly different. Figure 5.1 shows how a one-way ANOVA model in which the factor has three groups can be conceptualised.

If a factor has four groups, it is possible to conduct three independent two-sample *t*-tests, that is to test the mean values of group 1 vs 2, group 3 vs 4

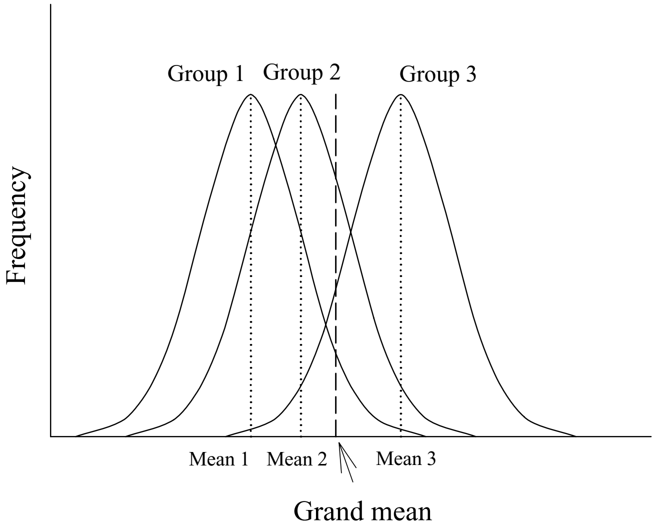

Figure 5.1 Concept of an ANOVA model.

and group 1 vs 4. However, this approach of conducting multiple two-sample t-tests increases the probability of obtaining a significant result merely by chance (a type I error). The probability of a type I error not occurring for each t-test is 0.95 (i.e. $1 - 0.05$). The three tests are independent, therefore the probability of a type I error not occurring over all three tests is $0.95 \times 0.95 \times 0.95$, or 0.86. Therefore, the probability of at least one type I error occurring over the three two-sample t-tests is 0.14 (i.e. $1 - 0.86$), which is higher than the P level set at 0.05.[1] A one-way ANOVA is therefore used to investigate the differences between several groups within a factor in one model and to reduce the number of pairwise comparisons that are made.

Within- and between-group variance

To interpret the output from an ANOVA model, it is important to have a concept of the mathematics used in conducting the test. In one-way ANOVA, the data are divided into their groups as shown in Figure 5.1 and a mean for each group is computed. Each mean value is considered to be the predicted value for that particular group of participants. In addition, a grand mean is calculated as shown in Table 5.2. The grand mean which is also shown in Figure 5.1, is the mean for all of the data and will only be the average of the three group means when the sample size in each group is equal.

Table 5.2 Means computed in one-way ANOVA

Group$_1$	Group$_2$	Group$_3$	Total sample
Group mean$_1$	Group mean$_2$	Group mean$_3$	Grand mean

The ANOVA analysis is then based on calculating the difference of each participant's observed value from their group mean, which is regarded as their predicted value, and also the difference from the grand mean. Thus, the following calculations are made for each participant:

$$\text{Within-group difference} = \text{group mean} - \text{observed measurement}$$
$$\text{Between-group difference} = \text{grand mean} - \text{observed measurement}$$

The within-group difference is the variation of each participant's measurement from their own group mean and is thought of as the explained variation. The between-group difference is the variation of each participant's measurement from the grand mean and is thought of as the unexplained variation. An important concept in ANOVA is that the within-group differences, which are also called residual or error values, are normally distributed.

In calculating ANOVA statistics, the within-group differences are squared and then summed to compute the within-group variance. The between-group differences are also squared and then summed to compute the between-group variance. The effect of squaring the values is to remove the effects of negative values, which would balance out the positive values.

The F value is calculated as the mean between-group variance divided by the mean within-group variance, that is the unexplained variance divided by the explained variance. Thus, the F value indicates whether the between-group variation is greater than would be expected by chance. The higher the F value, the more significant the ANOVA test because the groups (factors) are accounting for a higher proportion of the variance. Obviously, if more of the participants are closer to their group mean than to the grand mean, then the within-group variance will be lower than the between-group variance and F will be large. If the within-group variance is equal to the between-group variance, then F will be equal to 1 indicating that there is no significant difference in means between the groups of the factor.

If there are only two groups in a factor and only one factor, then a one-way ANOVA is equivalent to a two-sample t-test and F is equal to t^2. This relationship holds because t is calculated from the mean divided by the standard error (SE) in the same units as the original measurements whereas F is calculated from the variance, which is in squared units.

Research question

The spreadsheet **weights.sav** contains the data from a population sample of 550 term babies who had their weight recorded at 1 month of age. The babies also had their parity recorded, that is their birth order in their family.

Question:	Are the weights of babies related to their parity?
Null hypothesis:	That there is no difference in mean weight between groups defined by parity.
Variables:	Outcome variable = weight (continuous)
	Explanatory variable = parity (categorical, four groups)

The first statistics to obtain are the cell means and cell sizes. The number of children in each parity group can be obtained using the *Analyze → Descriptive Statistics → Frequencies* command sequences shown in Box 1.9.

Frequency table

Parity

		Frequency	Per cent	Valid per cent	Cumulative per cent
Valid	Singleton	180	32.7	32.7	32.7
	One sibling	192	34.9	34.9	67.6
	two siblings	116	21.1	21.1	88.7
	three or more siblings	62	11.3	11.3	100.0
	Total	550	100.0	100.0	

The Frequency table shows that the sample size of each group is large in that all cells have more than 30 participants. The cell size ratio is 62:192 or 1:3 and does not violate the ANOVA assumptions. Thus, the ANOVA model will be robust to some degrees of non-normality, outliers and unequal variances. However, it is still important to validate the ANOVA assumptions of normality and equal variances between groups. An awareness of any violations of these assumptions before running the model may influence how the results are interpreted, especially if any P values are of marginal significance. A small cell with a small variance compared to the other groups has the effect of inflating the F value, that is of increasing the chance of a type I error. On the other hand, a small cell with large variance compared to the other groups reduces the F value and increases the chance of a type II error.

Summary statistics and checks for normality can be obtained using the *Analyze → Descriptive Statistics → Explore* command sequence shown in Box 2.2 in Chapter 2. In this example, the dependent variable is weight and the factor list is parity. The plots that are most useful to request are the box plots, histograms and normality plots.

Descriptives

	Parity			**Statistic**	**Std. error**
Weight (kg)	Singleton	Mean		4.2589	0.04617
		95% confidence	Lower bound	4.1678	
		interval for mean	Upper bound	4.3501	
		5% trimmed mean		4.2588	
		Median		4.2500	
		Variance		0.384	
		Std. deviation		0.61950	
		Minimum		2.92	
		Maximum		5.75	
		Range		2.83	
		Inter-quartile range		0.9475	
		Skewness		0.046	0.181
		Kurtosis		−0.542	0.360
	One sibling	Mean		4.3887	0.04277
		95% confidence	Lower bound	4.3043	
		interval for mean	Upper bound	4.4731	
		5% trimmed mean		4.3709	
		Median		4.3250	
		Variance		0.351	
		Std. deviation		0.59258	
		Minimum		3.17	
		Maximum		6.33	
		Range		3.16	
		Inter-quartile range		0.8350	
		Skewness		0.467	0.175
		Kurtosis		0.039	0.349
	Two siblings	Mean		4.4601	0.05619
		95% confidence	Lower bound	4.3488	

Continued

	Parity			Statistic	Std. error
		interval for mean	Upper bound	4.5714	
		5% trimmed mean		4.4525	
		Median		4.4700	
		Variance		0.366	
		Std. deviation		0.60520	
		Minimum		3.09	
		Maximum		6.49	
		Range		3.40	
		Inter-quartile range		0.8225	
		Skewness		0.251	0.225
		Kurtosis		0.139	0.446
Weight (kg)	Three or more siblings	Mean		4.4342	0.06798
		95% confidence	Lower bound	4.2983	
		interval for mean	Upper bound	4.5701	
		5% trimmed mean		4.4389	
		Median		4.4450	
		Variance		0.287	
		Std. deviation		0.53526	
		Minimum		3.20	
		Maximum		5.48	
		Range		2.28	
		Inter-quartile range		0.7100	
		Skewness		–0.029	0.304
		Kurtosis		–0.478	0.599

The Descriptives table shows that means and medians for weight in each group are approximately equal and the values for skewness and kurtosis are all between +1 and −1 suggesting that the data are close to normally distributed. The variances in each group are 0.384, 0.351, 0.366 and 0.287 respectively. The variance ratio between the lowest and highest values is 0.287:0.384 which is 1:1.3.

Tests of Normality

		Kolmogorov–Smirnov[a]			**Shapiro–Wilk**		
	Parity	**Statistic**	***df***	**Sig.**	**Statistic**	***df***	**Sig.**
Weight (kg)	Singleton	0.038	180	0.200*	0.992	180	0.381
	One sibling	0.065	192	0.049	0.983	192	0.018
	Two siblings	0.059	116	0.200*	0.990	116	0.579
	Three or more siblings	0.070	62	0.200*	0.985	62	0.672

*This is a lower bound of the true significance.

[a] Lilliefors significance correction.

The Kolmogorov–Smirnov statistics in the Tests of Normality table suggest that the data for singletons, babies with two siblings, and babies with three or more siblings conform to normality with *P* values above 0.05. However, the data for babies with one sibling do not conform to a normal distribution because the *P* value of 0.049 is less than 0.05. Again, this is a conservative test of normality and failure to pass it does not always mean that ANOVA cannot be used unless other tests also indicate non-normality.

The histograms shown in Figure 5.2 confirm the tests of normality and show that the distribution for babies with one sibling has slightly spread tails so that

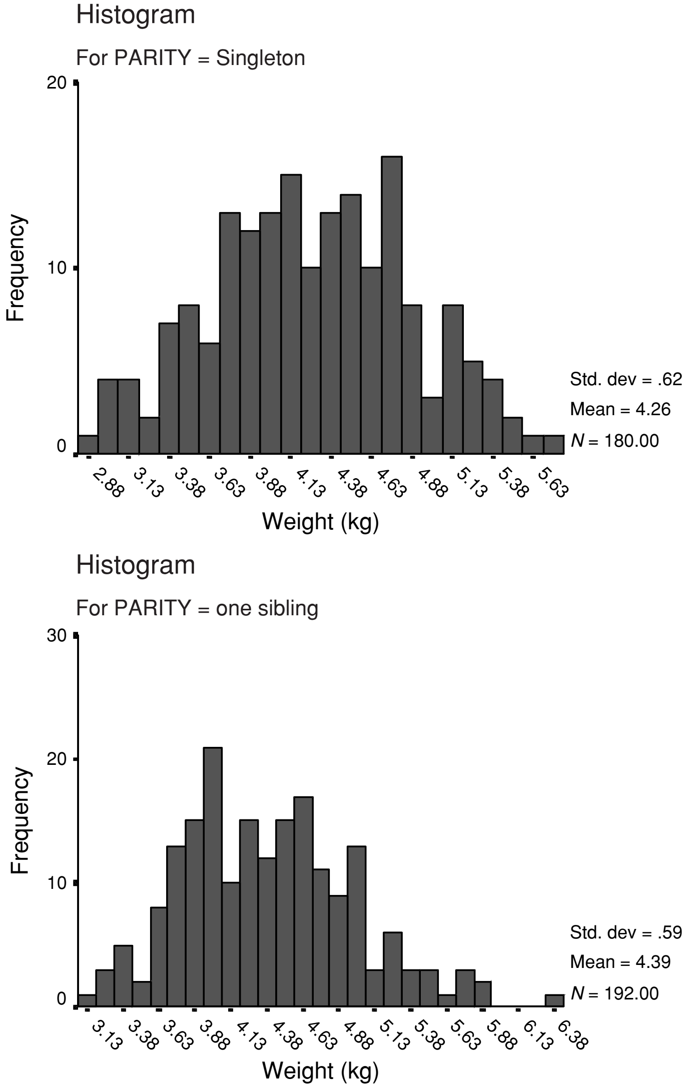

Figure 5.2 Plots of weight by parity.

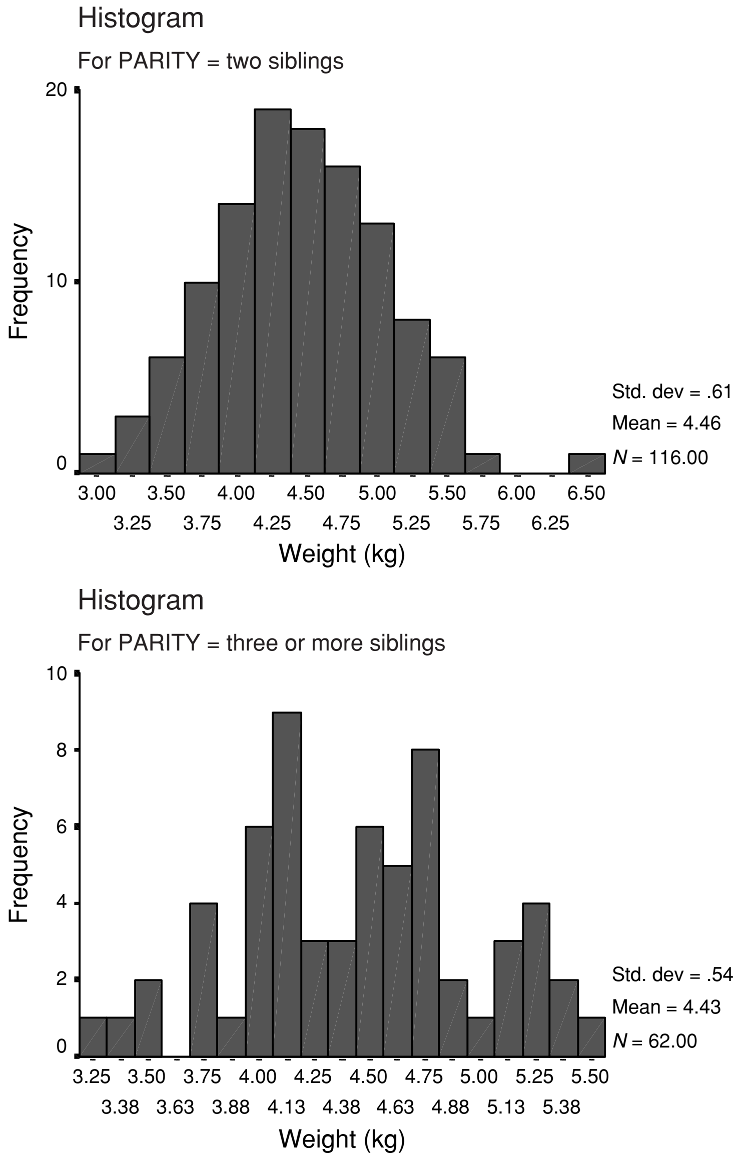

Figure 5.2 *Continued*

it does not conform absolutely to a bell shaped curve. The normal Q–Q plots shown in Figure 5.2 have small deviations at the extremities. The normal Q–Q plot for babies with one sibling deviates slightly from normality at both extremities. Although the histogram for babies with three or more siblings is not classically bell shaped, the normal Q–Q plot suggests that this distribution conforms to normality.

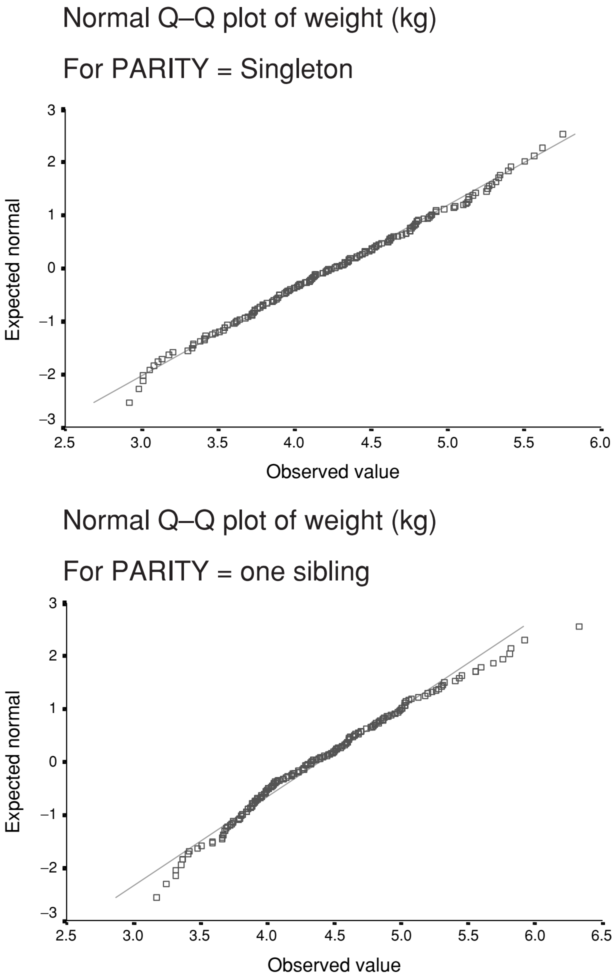

Figure 5.2 *Continued*

The box plots in Figure 5.2 indicate that there are two outlying values, one in the group of babies with one sibling and one in the group of babies with two siblings. It is unlikely that these outlying values, which are also univariate outliers, will have a large influence on the summary statistics and ANOVA result because the sample size of each group is large. However, the outliers should be confirmed as correct values and not data entry or data recording errors. Once they are verified as correctly recorded data points, the decision to include or omit outliers from the analyses is the same as for any other statistical tests. In a study with a large sample size, it is expected that there

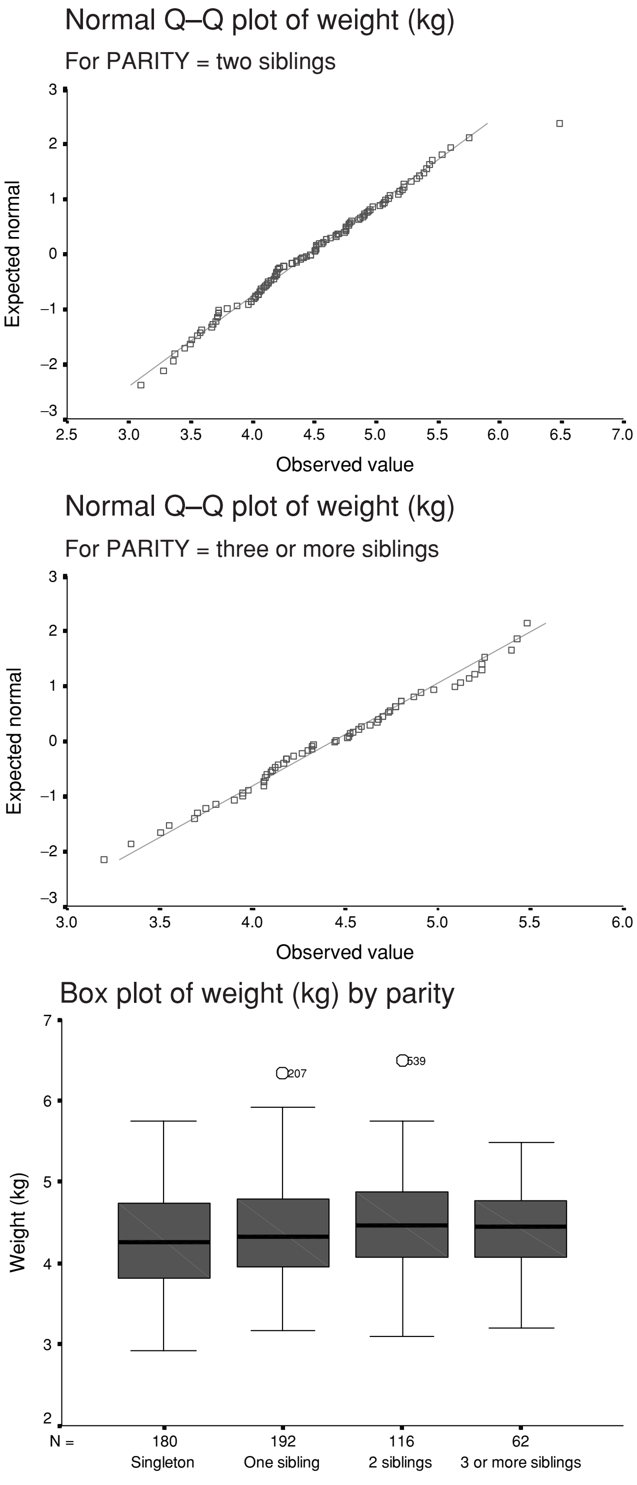

Figure 5.2 *Continued*

will be a few outliers (Chapter 3). In this data set, the outliers will be retained in the analyses and the extreme residuals will be examined to ensure that these values do not have undue influence on the results. The characteristics of the sample that need to be considered before conducting an ANOVA test and the features of the data set are summarised in Table 5.3.

Table 5.3 Characteristics of the data set

Characteristic	
Independence	Yes
Smallest cell size	62
Cell ratio	1:3
Variance ratio	1:1.3
Approximately normal distribution in each group	Yes
Number of outlying values	2
Number of univariate outliers	2

Running the one-way ANOVA

After the assumptions for using ANOVA have been checked and are validated, a one-way ANOVA can be obtained using the SPSS commands shown in Box 5.2.

Box 5.2 SPSS commands to obtain a one-way ANOVA

SPSS Commands
weights – SPSS Data Editor
    Analyze → Compare Means → One-Way ANOVA
One-Way ANOVA
    Highlight Weight and click over into Dependent List
    Highlight Parity and click over into Factor
    Click on Post-hoc
One-Way ANOVA: Post Hoc Multiple Comparisons
    Tick LSD, Bonferroni and Duncan, click Continue
One-Way ANOVA
    Click on Options
One-Way ANOVA: Options
    Tick Descriptive, Homogeneity of variance test, Means Plot, click Continue
One-Way ANOVA
    Click OK

One way

Descriptives
Weight (kg)

					95% confidence interval for mean			
	N	**Mean**	**Std. deviation**	**Std. error**	**Lower bound**	**Upper bound**	**Minimum**	**Maximum**
Singleton	180	4.2589	0.61950	0.04617	4.1678	4.3501	2.92	5.75
One sibling	192	4.3887	0.59258	0.04277	4.3043	4.4731	3.17	6.33
Two siblings	116	4.4601	0.60520	0.05619	4.3488	4.5714	3.09	6.49
Three or more siblings	62	4.4342	0.53526	0.06798	4.2983	4.5701	3.20	5.48
Total	550	4.3664	0.60182	0.02566	4.3160	4.4168	2.92	6.49

The summary statistics in the Descriptives table produced in a one-way ANOVA are identical to the statistics obtained using the command sequence *Analyze → Descriptive Statistics → Explore*. The descriptive statistics provided by the ANOVA commands show useful summary information but do not give enough details to check the normality of the distributions of weight in each group.

Test of Homogeneity of Variances
Weight (kg)

Levene statistic	***df1***	***df2***	**Sig.**
0.639	3	546	0.590

Homogeneity of variances is a term that is used to indicate that groups have the same or similar variances (Chapter 3). Thus, in the Test of Homogeneity of Variances table, the P value of 0.590 in the significance column, which is larger than the critical value of 0.05, indicates that the variance of each group is not significantly different from one another.

ANOVA
Weight (kg)

	Sum of squares	***df***	**Mean square**	***F***	**Sig.**
Between groups	3.477	3	1.159	3.239	0.022
Within groups	195.365	546	0.358		
Total	198.842	549			

The ANOVA table shows how the sum of squares is partitioned into between-group and within-group effects. The average of each sum of squares is needed to calculate the *F* value. Therefore, each sum of squares is divided by its respective degree of freedom (df) to compute the mean variance, which is called the mean square. The degrees of freedom for the between-group sum of squares is the number of groups minus 1, that is 4 − 1 = 3, and for the within-group sum of squares is the number of cases in the total sample minus the number of groups, that is 550 − 4 = 546.

In this model, the *F* value, which is the between-group mean square divided by the within-group mean square, is large at 3.239 and is significant at $P =$ 0.022. This indicates that there is a significant difference in the mean values of the four parity groups.

The amount of variation in weight that is explained by parity can be calculated as the between-group sum of squares divided by the total sum of squares to provide a statistic that is called eta squared as follows:

$$\begin{aligned}\text{Eta}^2 &= \text{Between-group sum of squares/Total sum of squares}\\ &= 3.477/198.842\\ &= 0.017\end{aligned}$$

This statistic indicates that only 1.7% of the variation in weight is explained by parity. Alternatively, eta^2 can be obtained using the commands *Analyze→ Compare Means→Means*, clicking on Options and requesting *ANOVA table and eta*. This will produce the same ANOVA table as above and include eta^2 but does not include a test of homogeneity or allow for post-hoc testing.

Post-hoc tests

Although the ANOVA statistics show that there is a significant difference in mean weights between parity groups, they do not indicate which groups are significantly different from one another. Specific group differences can be assessed using planned contrasts, which are decided before the ANOVA is run and which strictly limit the number of comparisons conducted[2]. Alternatively, post-hoc tests, which involve all possible comparisons between groups, can be used. Post-hoc tests are often considered to be data dredging and therefore inferior to the thoughtfulness of planned or *a priori* comparisons[3]. Some post-hoc tests preserve the overall type I error rate, but for other post-hoc tests the chance of a type I error increases with the number of comparisons made.

It is always better to run a small number of planned comparisons rather than a large number of unplanned post-hoc tests. Strictly speaking, the between-group differences that are of interest and the specific between-group comparisons that are made should be decided prior to conducting the ANOVA. In addition, planned and post-hoc tests should only be requested after the main ANOVA has shown that there is a statistically significant difference between groups. When the F test is not significant, it is unwise to explore whether there are any between-group differences[2].

A post-hoc test may consist of pairwise comparisons, group-wise comparisons or a combination of both. Pairwise comparisons are used to compare the differences between each pair of means. Group-wise comparisons are used to identify subsets of means that differ significantly from each other. Post-hoc tests also vary from being exceedingly conservative to simply conducting to multiple t-tests with no adjustment for multiple comparisons. A conservative test is one in which the actual significance is smaller than the stated significance level. Thus, conservative tests may incorrectly fail to reject the null hypothesis because a larger effect size between means is required for significance. Table 5.4 shows some commonly used post-hoc tests, their assumptions and the type of comparisons made.

Table 5.4 Types of comparisons produced by post-hoc tests

Post-hoc test	Requires equal group sizes	Group-wise subsets	Pairwise comparisons with a 95% CI
Equal variance assumed			
Conservative tests			
Scheffe	No	Yes	Yes
Tukey's honestly significant difference (HSD)	Yes	Yes	Yes
Bonferroni	No	No	Yes
Liberal tests			
Student–Newman–Keuls (SNK)	Yes	Yes	No
Duncan	Yes	Yes	No
Least significance difference (LSD)	Yes	No	Yes
Equal variance not assumed			
Games Howell	No	No	Yes
Dunnett's C	No	No	Yes

The choice of post-hoc test should be determined by equality of the variances, equality of group sizes and by the acceptability of the test in a particular research discipline. For example, Scheffe is often used in psychological medicine, Bonferroni in clinical applications and Duncan in epidemiological studies. The advantages of using a conservative post-hoc test have to be balanced against the probability of type II errors, that is missing real differences[4,5]. In the ANOVA test for the **weights.sav** data, the following post-hoc comparisons were requested:

Post-hoc tests

Multiple Comparisons
Dependent Variable: Weight (kg)

	(I) Parity	(J) Parity	Mean difference (I−J)	Std. error	Sig.	95% confidence interval	
						Lower bound	Upper bound
LSD	Singleton	One sibling	−0.1298*	0.06206	0.037	−0.2517	−0.0078
		Two siblings	−0.2011*	0.07122	0.005	−0.3410	−0.0612
		Three or more siblings	−0.1752*	0.08809	0.047	−0.3483	−0.0022
	One sibling	Singleton	0.1298*	0.06206	0.037	0.0078	0.2517
		Two siblings	−0.0714	0.07034	0.311	−0.2096	0.0668
		Three or more siblings	−0.0455	0.08738	0.603	−0.2171	0.1261
	Two siblings	Singleton	0.2011*	0.07122	0.005	0.0612	0.3410
		One sibling	0.0714	0.07034	0.311	−0.0668	0.2096
		Three or more siblings	0.0259	0.09410	0.783	−0.1590	0.2107
	Three or more siblings	Singleton	0.1752*	0.08809	0.047	0.0022	0.3483
		One sibling	0.0455	0.08738	0.603	−0.1261	0.2171
		Two siblings	−0.0259	0.09410	0.783	−0.2107	0.1590
Bonferroni	Singleton	One sibling	−0.1298	0.06206	0.222	−0.2941	0.0346
		Two siblings	−0.2011*	0.07122	0.029	−0.3897	−0.0126
		Three or more siblings	−0.1752	0.08809	0.283	−0.4085	0.0580
	One sibling	Singleton	0.1298	0.06206	0.222	−0.0346	0.2941
		Two siblings	−0.0714	0.07034	1.000	−0.2577	0.1149
		Three or more siblings	−0.0455	0.08738	1.000	−0.2769	0.1859
	Two siblings	Singleton	0.2011*	0.07122	0.029	0.0126	0.3897
		One sibling	0.0714	0.07034	1.000	−0.1149	0.2577
		Three or more siblings	0.0259	0.09410	1.000	−0.2233	0.2751
	Three or more siblings	Singleton	0.1752	0.08809	0.283	−0.0580	0.4085
		One sibling	0.0455	0.08738	1.000	−0.1859	0.2769
		Two siblings	−0.0259	0.09410	1.000	−0.2751	0.2233

*The mean difference is significant at the 0.05 level.

The Multiple Comparisons table shows pairwise comparisons generated using the least significance difference (LSD) and Bonferroni post-hoc tests. The LSD test is the most liberal post-hoc test because it performs all possible tests between means. This test is not normally recommended when more than three groups are being compared or when there are unequal variances or cell sizes. With no adjustments made for multiple tests or comparisons, the results of the LSD test amount to multiple *t*-testing and has been included here only for comparison with the Bonferroni test.

The Multiple Comparisons table shows the mean difference between each pair of groups, the significance and the confidence intervals around the difference in means between groups. SigmaPlot can be used to plot the LSD mean differences and 95% confidence intervals as a scatter plot with horizontal error bars using the commands shown in Box 3.6 to obtain Figure 5.3. This figure shows that three of the comparisons have error bars that cross the zero line of no difference, and the differences are not statistically significant using the LSD test. The remaining three comparisons do not cross the zero line of no difference and are statistically significant as indicated by the *P* values in the Multiple Comparisons table.

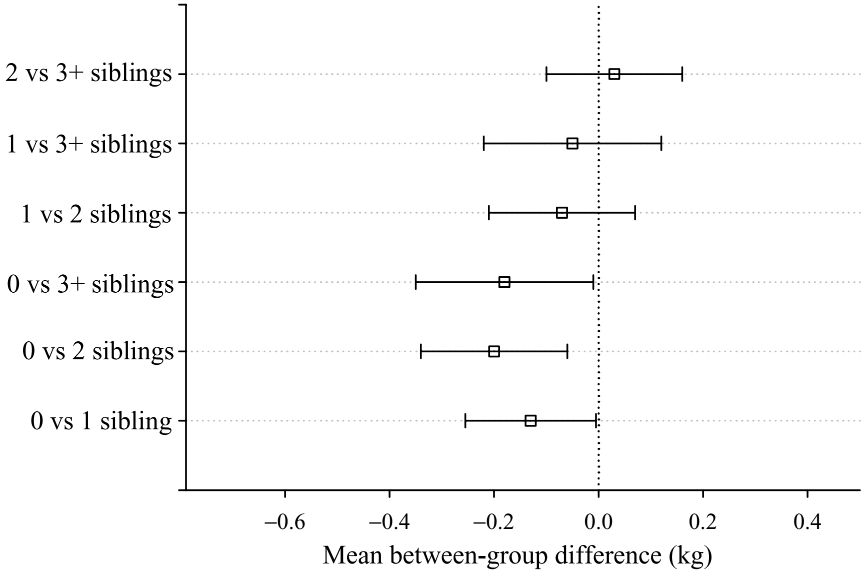

Figure 5.3 Between-group comparisons with no adjustment for multiple testing.

The Bonferroni post-hoc comparison is a conservative test in which the critical *P* value of 0.05 is divided by the number of comparisons made. Thus, if five comparisons are made, the critical value of 0.05 is divided by 5 and the adjusted new critical value is $P = 0.01$. In SPSS the *P* levels in the Multiple Comparisons table have already been adjusted for the number of multiple comparisons. Therefore, each *P* level obtained from a Bonferroni test in the Multiple Comparisons table should be evaluated at the critical level of 0.05.

By using the Bonferroni test, which is a conservative test, the significant differences between some groups identified by the LSD test are now non-significant. The mean values are identical but the confidence intervals are adjusted so that they are wider as shown in Figure 5.4. The 95% error bars show that only one comparison does not cross the zero line of difference compared to three comparisons using the LSD test.

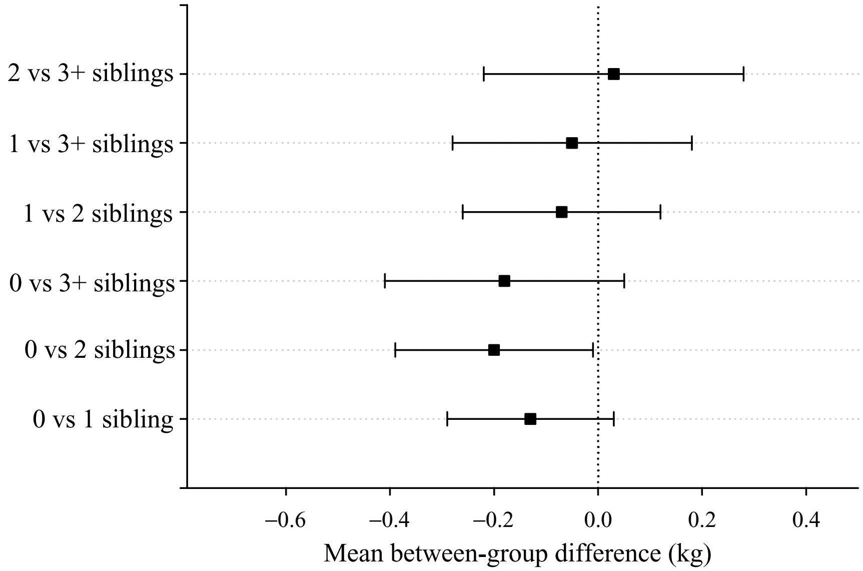

Figure 5.4 Between-group comparisons using Bonferroni corrected confidence intervals.

Homogeneous subsets

Weight (kg)

			Subset for alpha = 0.05	
	Parity	***N***	**1**	**2**
Duncan[a,b]	Singleton	180	4.2589	
	One sibling	192	4.3887	4.3887
	Three or more siblings	62		4.4342
	Two siblings	116		4.4601
	Sig.		0.104	0.403

Means for groups in homogeneous subsets are displayed.

[a] Uses harmonic mean sample size = 112.633.

[b] The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.

The Duncan test shown in the Homogeneous Subsets table is one of the more liberal post-hoc tests. Under this test, there is a progressive comparison between the largest and smallest mean values until a difference that is not significant at the $P < 0.05$ level is found and the comparisons are stopped. In this way, the number of comparisons is limited. The output from this test is presented as subsets of groups that are not significantly different from one another. The between-group P value (0.05) is shown in the top row of the Homogenous subtests table and the within-group P values at the foot of the columns. Thus in the table, the mean values for groups of singletons and babies with one sibling are not significantly different from one another with a P value of 0.104. Similarly, the mean values of groups with one sibling, two siblings, or three or more siblings are not significantly different from one another with a P value of 0.403. Singletons do not appear in the same subset as babies with two siblings or with three or more siblings which indicates that the mean weight of singletons is significantly different from these two groups at the $P < 0.05$ level.

The means plot provides a visual presentation of the mean value for each group. The means plot shown in Figure 5.5 indicates that there is a trend for weight to increase with increasing parity and helps in the interpretation of the post-hoc tests. It also shows why the group with one sibling is not significantly

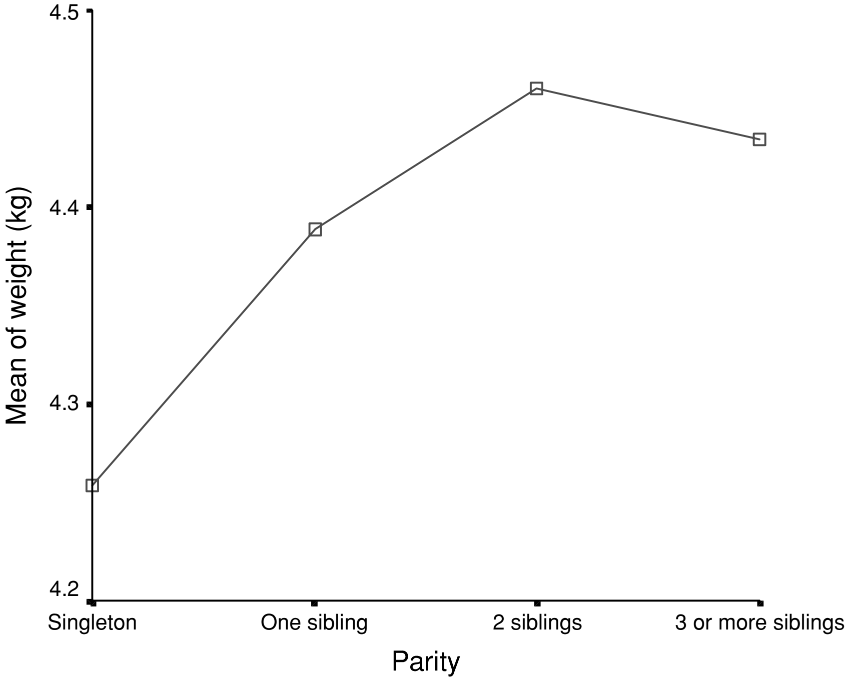

Figure 5.5 Means plot of weight by parity.

different from singletons or babies with two siblings or with three or more siblings, and why singletons are significantly different from the groups with two siblings or with three or more siblings.

If the means plot shown in Figure 5.5 was to be published, it would be best plotted in SigmaPlot with 95% confidence intervals around each mean value included to help interpret the between-group differences. Also, the line connecting the mean value of each group should be removed because the four groups are independent of one another.

Trend test

The increase in weight with increasing parity suggests that it is appropriate to test whether there is a significant linear trend for weight to increase across the groups within this factor. A trend test can be performed by re-running the one-way ANOVA and ticking the Polynomial option in the Contrasts box with the Degree: Linear (default) option used. As the polynomial term implies, an equation is calculated across the model.

One way

ANOVA
Weight (kg)

			Sum of squares	*df*	Mean square	*F*	Sig.
Between groups	(Combined)		3.477	3	1.159	3.239	0.022
	Linear term	Unweighted	1.706	1	1.706	4.768	0.029
		Weighted	2.774	1	2.774	7.754	0.006
		Deviation	0.703	2	0.351	0.982	0.375
Within groups			195.365	546	0.358		
Total			198.842	549			

If each of the parity cells had the same number of cases then the unweighted linear term would be used to assess the significance of the trend. However, the cell sizes are unequal and therefore the weighted linear term is used. The table shows that the weighted linear term sum of squares is significant at the $P = 0.006$ level indicating that there is a significant trend for mean weight to increase as parity or the number of siblings increases.

Reporting the results

In addition to presenting the between-group comparisons shown in Figure 5.3, the results from the one-way ANOVA can be summarised as shown in Table 5.5. When describing the table it is important to include details stating that weight was approximately normally distributed in each group and that the group sizes were all large (minimum 62) with a cell size ratio of 1:3 and a variance ratio of 1:1.3. The significant difference in weight at 1 month between children with different parities can be described as $F = 3.24$, $df = 3$, 546, $P = 0.022$ with a significant linear trend for weight to increase with increasing parity ($P = 0.006$). The degrees of freedom are conventionally shown as the between-group and within-group degrees of freedom separated with a comma. Although the inclusion of the F value and degrees of freedom is optional since their only interpretation is the P value, some journals request that they are reported.

Table 5.5 Reporting results from a one-way ANOVA

Parity	*N*	Mean (SD)	*F (df)*	*P* value	*P* value trend
Singletons	180	4.26 (0.62)	3.24 (3, 546)	0.022	0.006
One sibling	192	4.39 (0.59)			
Two siblings	116	4.46 (0.61)			
Three or more siblings	62	4.43 (0.54)			

When designing the study, only one post-hoc test should be planned and conducted if the ANOVA was significant. If the Bonferroni post-hoc test had been conducted, it could be reported that the only significant difference in mean weights was between singletons and babies with two siblings ($P = 0.029$) with no significant differences between any other groups.

If Duncan's post-hoc test had been conducted, it could be reported that babies with two siblings and babies with three or more siblings were significantly heavier than singletons ($P < 0.05$). However, babies with one sibling did not have a mean weight that was significantly different from either singletons ($P = 0.104$) or from babies with two siblings, or with three or more siblings ($P = 0.403$).

Factorial ANOVA models

A factorial ANOVA is used to test for differences in mean values between groups when there are two or more factors, or explanatory variables, with two or more groups each included in a single multivariate analysis. In SPSS, factorial ANOVA is accessed through the *Analyze → General Linear Models → Univariate* command sequence. The term univariate may seem confusing in this context but in this case refers to there being only one outcome variable rather than only one explanatory factor.

In a factorial ANOVA, the data are divided into cells according to the number of participants in each group of each factor stratified by the other factors. The more explanatory variables that are included in a model, the greater the likelihood of creating small or empty cells. The cells can be conceptualised as shown in Table 5.6. The number of cells in a model is calculated by multiplying the number of groups in each factor. For a model with three factors that have three, two and four groups respectively as shown in Table 5.6, the number of cells is 3 × 2 × 4, or 24 cells in total.

Table 5.6 Cells in the analysis of a model with three factors (three-way ANOVA)

FACTOR 1	**Group 1**		**Group 2**		**Group 3**	
FACTOR 2	**Group 1**	**Group 2**	**Group 1**	**Group 2**	**Group 1**	**Group 2**
FACTOR 3						
Group 1	$m_{1,1,1}$	$m_{2,1,1}$	$m_{1,2,1}$	$m_{2,2,1}$	$m_{1,3,1}$	$m_{2,3,1}$
2	$m_{1,1,2}$	$m_{2,1,2}$	$m_{1,2,2}$	$m_{2,2,2}$	$m_{1,3,2}$	$m_{2,3,2}$
3	$m_{1,1,3}$	$m_{2,1,3}$	$m_{1,2,3}$	$m_{2,2,3}$	$m_{1,3,3}$	$m_{2,3,3}$
4	$m_{1,1,4}$	$m_{2,1,4}$	$m_{1,2,4}$	$m_{2,2,4}$	$m_{1,3,4}$	$m_{2,3,4}$

In factorial ANOVA, the within-group differences are calculated as the distance of each participant from its cell mean rather than from the group mean as in one-way ANOVA. However, the between-group differences are again calculated as the difference of each participant from the grand mean, that is the mean of the entire data set. As with one-way ANOVA, all of the differences are squared and summed, and then the mean square is calculated.

Fixed factors, interactions and random factors

Both fixed and random effects can be incorporated in factorial ANOVA models. Factorial ANOVA is mostly used to examine the effects of fixed factors which are factors in which all possible groups are included, for example males and females or number of siblings. When using fixed factors, the differences between the specified groups are the statistics of interest.

Sometimes the effect of one fixed factor is modified by another fixed factor, that is it interacts with it. The presence of a significant interaction between two or more factors or between a factor and a covariate can be tested in a factorial ANOVA model. The interaction term is computed as a new variable by multiplying the factors together and then included in the model or can be requested on an SPSS option.

Factors are considered to be random when only a sample of a wider range of groups is included. For example, factors may be classified as having random effects when only three or four ethnic groups are represented in the sample but the results will be generalised to all ethnic groups in the community. In this case, only general differences between the groups are of interest because the results will be used to make inferences to all possible ethnic groups rather than to only the groups in the sample.

It is important to classify groups as random factors if the study sample was selected by recruiting, for example, specific sports teams, schools or doctors' practices and the results will be generalised to all sports teams, schools or doctors' practices or if different sports teams, schools or doctors' practices would be selected in the future. In these types of study designs, there is a cluster sampling effect and the group is entered into the model as a random factor.

The classification of factors as fixed or random effects has implications for interpreting the results of the ANOVA. In random effect models, any unequal variance between cells is less important when the numbers in each cell are equal. However, when there is increasing inequality between the numbers in each cell, then differences in variance become more problematic. The use of fixed or random effects can give very different *P* values because the *F* statistic is computed differently. For fixed effects, the *F* value is calculated as the between-group mean square divided by the error mean square whereas for random effects, the *F* value is calculated as the between-group mean square divided by the interaction mean square.

Research question

Differences in weights between genders can be tested using a two-sample *t*-test and differences between different parities were tested in the previous example using a one-way ANOVA. However, maternal education status (Year 10 school, Year 12 school or university) in addition to gender and parity can be tested together as explanatory factors in a three-way ANOVA model. These factors are all fixed factors.

Question:	Are the weights of babies related to their gender, parity or maternal level of education?
Null hypothesis:	That there is no difference in mean weight between groups defined according to gender, parity and level of education
Variables:	Outcome variable = weight (continuous) Explanatory variables = gender (categorical, two groups), parity (categorical, four groups) and maternal education (categorical, three groups)

The number of cells in the ANOVA model will be 2 (gender) × 3 (maternal education) × 4 (parity), or 24 cells. First, the summary statistics need to be obtained to verify that there are an adequate number of babies in each cell. This can be achieved by splitting the file by gender which has the smallest number of groups and then generating two tables of parity by maternal education as shown in Box 5.3.

Box 5.3 SPSS commands to obtain cell sizes

SPSS Commands

weights – SPSS Data Editor

  Data → Split File

Split File

  Tick ‘Organise output by groups’

  Highlight Gender and click into ‘Groups Based on’ box

  Click OK

weights – SPSS Data Editor

  Analyze → Descriptive Statistics → Crosstabs

Crosstabs

  Highlight Maternal education and click into Rows

  Highlight Parity and click into Columns

  Click OK

Gender = male

Maternal Education * Parity Crosstabulation
Count

		Parity				
		Singleton	**One sibling**	**Two siblings**	**Three or more siblings**	**Total**
Maternal education	year 10	15	40	26	17	98
	year 12	22	16	8	4	50
	Tertiary	55	42	22	8	127
Total		92	98	56	29	275

[a] Gender = male.

Gender = female

Maternal Education * Parity Crosstabulation
Count

		Parity				
		Singleton	**One sibling**	**Two siblings**	**Three or more siblings**	**Total**
Maternal education	year 10	24	36	21	19	100
	year 12	19	15	13	2	49
	Tertiary	45	43	26	12	126
Total		88	94	60	33	275

[a] Gender = Female.

The Crosstabulations tables show that even with a large sample size of 550 babies, including three factors in the model will create some small cells with less than 10 cases and that there is a large cell imbalance. For males, the cell size ratio is 4:55, or 1:14, and for females the cell size ratio is 2:45, or 1:23. Without maternal education included, all cell sizes as indicated by the Total row and Total column totals are quite large. To increase the small cell sizes, it would make sense to combine the groups of two siblings and three or more siblings. This combining of cells is possible because the theory is valid and because the one-way ANOVA showed that the means of these two groups are not significantly different from one another. By combining these groups, the smallest cells will be larger at 8 + 4 or 12 for males and 13 + 2 or 15 for females. The cell ratios will then be 12:55, or 1:4.6 for males and 15:45, or 1:3 for females. The ratio for males is close to the assumption of 1:4 and within this assumption for females.

To combine the parity groups, the re-code commands shown in Box 1.10 can be used after removing the Split file option as shown in Box 5.4.

Box 5.4 SPSS commands to remove split file

SPSS Commands

```
weights – SPSS Data Editor
            Data → Split File
            Tick 'Analyse all cases, do not create groups'
            Click OK
```

The SPSS commands to obtain summary means for parity and maternal education in males and females separately are shown in Box 5.5.

Box 5.5 SPSS commands to obtain summary means

SPSS Commands

```
weights – SPSS Data Editor
            Analyze → Compare Means → Means
Means
            Highlight Weight and click into Dependent List
            Highlight Gender, Maternal education and Parity recoded (3 levels),
                click into Independent List
            Click OK
```

Means

Weight (kg) * Gender

Weight (kg)

Gender	Mean	*N*	Std. deviation
Male	4.5923	275	0.62593
Female	4.1405	275	0.48111
Total	4.3664	550	0.60182

Weight (kg) * Maternal Education
Weight (kg)

Maternal education	Mean	N	Std. deviation
Year10	4.3529	198	0.55993
Year12	4.4109	99	0.69464
Tertiary	4.3596	253	0.59611
Total	4.3664	550	0.60182

Weight (kg) * Parity Recoded (Three Levels)
Weight (kg)

Parity re-coded (Three levels)	Mean	N	Std. deviation
Singleton	4.2589	180	0.61950
One sibling	4.3887	192	0.59258
Two or more siblings	4.4511	178	0.58040
Total	4.3664	550	0.60182

The Means tables show mean values in each group for each factor. There is a difference of 4.59 – 4.14, i.e. 0.45 kg between genders, a difference of 4.41 – 4.35, i.e. 0.06 kg between the highest and lowest maternal education groups and a difference of 4.45 – 4.26, i.e. 0.19 kg between the highest and lowest parity groups. These are not effect sizes in units of the standard deviations so the differences cannot be directly compared. In ANOVA, effect sizes can be calculated but the number of groups and the pattern of dispersion of the mean values across the groups need to be taken into account[6]. However, the absolute differences show that the largest difference is for gender followed by parity and that there is an almost negligible difference for maternal education. The effect of maternal education is so small that it is unlikely to be a significant predictor in a multivariate model.

The summary statistics can also be used to verify the cell size and variance ratios. A summary of this information validates the model and helps to interpret the output from the three-way ANOVA. The cell size ratio when parity is re-coded into three cells has been found to be adequate. The variance ratio for each factor, for example for parity, can be calculated by squaring the standard deviations from the Means table. For parity, the variance ratio is $(0.58)^2$:$(0.62)^2$ or 1:1.14.

Next, the distributions of the variables should be checked for normality using the methods described in Chapter 2 and for one-way ANOVA. The largest difference between mean values is between genders, therefore it is important to examine the distribution for each gender to identify any outlying values or outliers. In fact, the distribution of each group for each factor should be checked for the presence of any outlying values or univariate outliers. The output is not included here but the analyses should proceed in the knowledge that there are no influential outliers and no significant deviations from normality for any variable in the model.

The commands for running a three-way ANOVA to test for the effects of gender (two groups), parity (three groups) and maternal education (three groups) on weight and to test for a trend for weight to increase with increasing parity are shown in Box 5.6.

Box 5.6 SPSS commands to obtain a three-way ANOVA

SPSS Commands

```
weights – SPSS Data Editor
        Analyze → General Linear Model → Univariate
Univariate
        Highlight Weight and click into Dependent Variable
        Highlight Gender, Maternal education and Parity recoded (3 levels) and
          click into Fixed Factor(s)
        Click on Model
Univariate: Model
        Click on Custom
        Under Build Term(s) pull down menu and click on Main effects
        Highlight gender, education and parity1 and click over into Model
        Sum of squares: Type III on pull down menu (default)
        Tick Include intercept in model (default), click Continue
Univariate
        Click on Contrasts
Univariate Contrasts
        Factors: Highlight parity1
        Change Contrasts: pull down menu, highlight Polynomial, click Change,
        click Continue
Univariate
        Click on Plots
Univariate: Profile Plots
        Highlight gender, click into Horizontal Axis
        Highlight parity1, click in Separate Lines, click Add, click Continue
Univariate
        Click on Options
Univariate: Options
        Highlight gender, education and parity1 and click into 'Display
        Means for'
        Tick 'Compare main effects'
```

Confidence interval adjustment: LSD (none)(default)
Click Continue
Univariate
Click OK

Univariate analysis of variance

Tests of Between-Subject Effects
Dependent Variable: Weight (kg)

Source	Type III Sum of Squares	*df*	Mean square	*F*	Sig.
Corrected model	32.613[a]	5	6.523	21.346	0.000
Intercept	9012.463	1	9012.463	29494.120	0.000
GENDER	28.528	1	28.528	93.361	0.000
EDUCATIO	0.604	2	0.302	0.989	0.373
PARITY1	4.327	2	2.164	7.080	0.001
Error	166.229	544	0.306		
Total	10684.926	550			
Corrected total	198.842	549			

[a] R squared = 0.164 (adjusted R squared = 0.156).

A three-way ANOVA shown in the Tests of Between-Subject Effects table is similar to a regression model. In the table, the first two rows show the Corrected Model and Intercept and indicate that the factors are significant predictors of weight. The corrected model sum of squares divided by the corrected total sum of squares, that is 32.613/198.842 or 0.164, is the variation that can be explained by the model and is the R squared value shown in the footnote. This value indicates that gender, maternal education and parity together explain 0.164 or 16.4% of the variation in weight. This is considerably higher than the 1.7% explained by parity only in a previous model.

The F values are the within-group mean square divided by the error mean square. The F values for the three factors show that both gender and parity are significant predictors of weight at 1 month with $P < 0.0001$ and $P = 0.001$ respectively, but that maternal educational status is not a significant predictor with $P = 0.373$. After combining two of the parity groups and adjusting for gender differences in the parity groups, the significance of parity in predicting weight has increased to $P = 0.001$ compared with $P = 0.022$ obtained from the one-way ANOVA previously conducted.

The sums of squares for the model, intercept, factors and the error term when added up manually equal 9244.764. This is less than the total sum of squares of 10 684.926 shown in the table, which also includes the sum of squares for all possible interactions between factors in the model, even though the inclusion of interactions was not requested.

Custom Hypothesis Tests

Contrast Results (K matrix)

Parity recoded (three levels)			Dependent variable
Polynomial contrast[a]			**Weight (kg)**
Linear	Contrast estimate		0.157
	Hypothesised value		0
	Difference (estimate − hypothesised)		0.157
	Std. error		0.042
	Sig.		0.000
	95% confidence interval	Lower bound	0.074
	for difference	Upper bound	0.240
Quadratic	Contrast estimate		−0.025
	Hypothesised value		0
	Difference (estimate − hypothesised)		−0.025
	Std. error		0.040
	Sig.		0.542
	95% confidence interval	Lower bound	−0.104
	for difference	Upper bound	0.055

[a] Metric = 1.000, 2.000, 3.000.

The polynomial linear contrast in the Contrast Results table shows that there is again a significant trend for weight to increase with parity at the $P < 0.0001$ level. The subscript to this table indicates that the outcome is being assessed over the three parity groups, that is the groups labelled 1, 2 and 3. The quadratic term is not relevant because there is no evidence to suggest that the relationship between weight and parity is curved rather than linear, and consistent with this, the quadratic contrast is not significant.

Estimated Marginal Means

Estimates
Dependent Variable: Weight (kg)

			95% confidence interval	
Gender	**Mean**	**Std. error**	**Lower bound**	**Upper bound**
Male	4.603	0.035	4.535	4.672
Female	4.148	0.035	4.079	4.216

The Estimated Marginal Means table shows mean values adjusted for the other factors in the model, that is the predicted mean values. Marginal means

Pairwise Comparisions
Dependent Variable: Weight (kg)

(I) gender	(J) gender	Mean difference (I−J)	Std. error	Sig.[a]	95% Confidence Interval for Difference[a]	
					Lower bound	Upper bound
Male	Female	0.456*	0.047	0.000	0.363	0.548
Female	Male	−0.456*	0.047	0.000	−0.548	−0.363

Based on estimated marginal means.

*The mean difference is significant at the 0.05 level.

[a] Adjustment for multiple comparisions: least significant difference (equivalent to no adjustments).

Univariate Tests
Dependent Variable: Weight (kg)

	Sum of squares	*df*	Mean square	*F*	Sig.
Contrast	28.528	1	28.528	93.361	0.000
Error	166.229	544	0.306		

The *F* tests the effect of gender. This test is based on the linearly independent pairwise comparisions among the estimated marginal means.

that are similar to the unadjusted mean values provide evidence that the model is robust. If the marginal means change by a considerable amount after adding an additional factor to the model, then the added factor is an important confounder or covariate. The significance of the comparisons in the Pairwise Comparisons table is based on a *t* value, that is the mean difference/SE, for the difference in marginal means without any adjustment for multiple comparisons.

In this model, the marginal means are adjusted for differences in the distribution of parity and maternal education in the two gender groups. The standard errors are identical in the two groups because the pooled data for all cases are used to compute a single estimate of the standard error. For this reason, it is important that the assumptions of equal variance and similar cell sizes in all groups are met. The marginal mean for males is 4.603 kg compared to a mean of 4.592 kg in the unadjusted analysis, and for females is 4.148 kg compared to 4.141 kg in the unadjusted analysis. Thus, the difference between genders in the adjusted ANOVA analysis is 0.456 kg compared with a difference of 0.452 kg that can be calculated from the previous Means table.

Pairwise comparisons for maternal education and parity were also requested although they have not been included here.

The Profile plot shown in Figure 5.6 indicates that the relative values in mean weights between groups defined according to parity are the same for both genders. In the plot, if the lines cross one another this would indicate an interaction between factors. However, in Figure 5.6, the lines are parallel which indicates that there is no interaction between gender and parity. Interactions are discussed in more detail in Chapter 6.

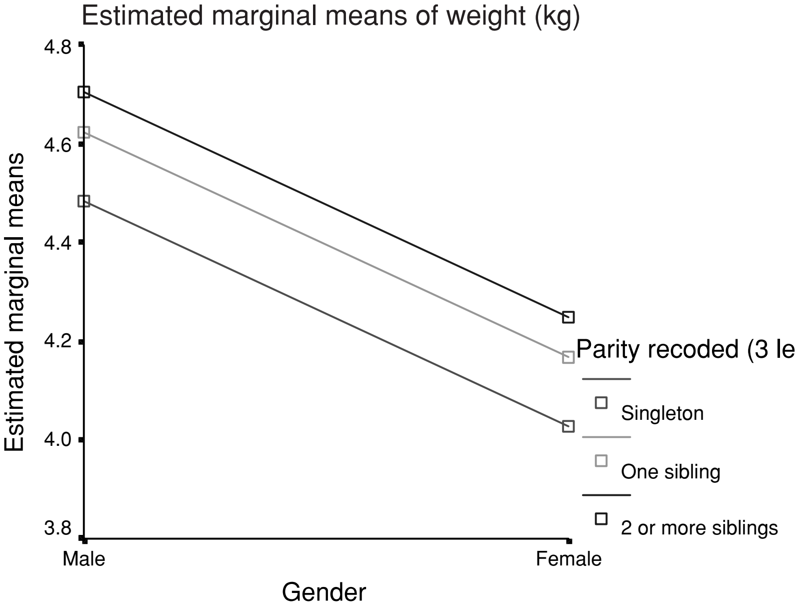

Figure 5.6 Profile plot of marginal means of weight by gender and parity.

Reporting the results

The results from the three-way ANOVA can be presented as shown in Table 5.7.

Table 5.7 Mean weights of babies at 1 month of age by gender, parity and maternal education

	N	Weight (kg) Mean (SD)	*F* (*df*)	*P* value	*P* value trend
Gender					
Males	275	4.59 (0.63)	93.36 (1, 544)	<0.0001	–
Females	275	4.14 (0.48)			
Parity					
Singletons	180	4.26 (0.62)	7.08 (2, 544)	0.001	<0.0001
One sibling	192	4.39 (0.59)			
Two or more siblings	178	4.45 (0.58)			
Maternal education					
Year 10 school	198	4.35 (0.56)	0.99 (2, 544)	0.373	–
Year 12 school	99	4.41 (0.69)			
Tertiary education	253	4.36 (0.60)			

The results could be described as follows: 'Table 5.7 shows the unadjusted mean weights of babies at 1 month of age by group. The *F* and *P* values were derived from a three-way ANOVA. The cell size was within the assumption of 1:4 for females and close to this assumption for males and the variance ratio was less than 1:2. There was a significant difference in weight between males and females and between groups defined according to parity, but not between groups defined according to maternal education status. A polynomial contrast indicated that the linear trend for weight to increase with parity was significant at $P < 0.0001$. Pairwise contrasts showed that the difference in marginal means between males and females was 0.46 kg (95% CI 0.36, 0.55). In addition, the difference in marginal means between singletons and babies with one sibling was statistically significant at −0.14 kg (95% CI −0.25, −0.03, $P = 0.015$) and the difference between singletons and babies with two or more siblings were statistically significant at −0.22 kg (95% CI − 0.34, −0.11, $P < 0.0001$). Profile plots indicated that there was no interaction between gender and parity'.

Analysis of covariance

Analysis of covariance (ANCOVA) is used when it is important to examine group differences after adjusting the outcome variable for a continuously distributed explanatory variable (covariate). The ANCOVA analysis first produces a regression of the outcome on the covariate and then adjusts the cell means for the effect of the covariate. Adjusting for a covariate has the effect of reducing the residual (error) term by reducing the amount of noise in the model. As in regression, it is important that the association between the outcome and the covariate is linear. In ANCOVA, the residual terms are the distances of each individual from the regression line and not from the cell mean, thus the residual distances are smaller than in ANOVA.

The assumptions for ANCOVA are identical to the assumptions for ANOVA but the additional assumptions shown in Box 5.7 must also be met.

Box 5.7 Additional assumptions for ANCOVA

The following assumptions for ANCOVA must be met in addition to the assumptions shown in Box 5.1 for ANOVA:

- the measurement of the covariate is reliable
- if there is more than one covariate, there is low collinearity between covariates
- the association between the covariate and the outcome is linear
- there is homogeneity of the regression, that is the slopes across the data in each cell are the same as the slope in the total sample
- there is no interaction between the covariate and the factors
- there are no multivariate outliers

In building the ANCOVA model, the choice of covariates must be made carefully and should be limited to covariates that can be measured reliably.

Few covariates are measured without any error but unreliable covariates lead to a loss of statistical power. Covariates such as age and height can be measured reliably but other covariates such as reported hours of sleep or time spent exercising may be subject to significant reporting bias.

It is also important to limit the number of covariates to variables that are not significantly related to one another. As in all multivariate models, collinearity, that is a significant association or correlation between explanatory variables, can result in an unstable model and unreliable estimates of effect, which can be difficult to interpret. Ideally, the correlation (r) between covariates should be low.

Research question

Weight is related to the length of a baby and therefore it makes sense to use ANCOVA to test whether the significant differences in weight between gender and parity groups are maintained after adjusting for length. In testing this, length is added into the model as a covariate. The SPSS commands for running an ANCOVA model are shown in Box 5.8. Maternal education has been omitted from this model because the previous three-way ANOVA showed that this variable does not have a significant relationship with babies' weights.

Box 5.8 SPSS commands for obtaining an ANCOVA model

SPSS commands

```
weights – SPSS Data Editor
        Analyze → General Linear Model → Univariate
Univariate
        Click on Reset
        Highlight Weight and click into Dependent Variable
        Highlight Gender and Parity recoded (3 levels) and click into Fixed Factors
        Highlight Length, click into Covariate(s)
        Click on Model
Univariate: Model
        Click on Custom
        Under Build Term(s) pull down menu and click on Main effects
        Highlight gender, parity1 and length and click over into Model
        Sum of squares: Type III on pull down menu (default)
        Tick Include intercept in model (default), click Continue
Univariate
        Click on Contrasts
Univariate Contrasts
        Factors: Highlight parity1
        Change Contrast: pull down menu, highlight Polynomial, click Change,
        click Continue
Univariate
        Click on Options
Univariate: Options
```

Highlight gender and Parity1, click into 'Display Means for'
Tick 'Compare main effects'
Confidence interval adjustment: using LSD (none)(default)
Click Continue
Univariate
Click OK

Tests of Between-Subject Effects
Dependent Variable: Weight (Kg)

Source	Type III sum of squares	*df*	Mean square	*F*	Sig.
Corrected model	111.164[a]	4	27.791	172.747	0.000
Intercept	20.805	1	20.805	129.322	0.000
GENDER	8.378	1	8.378	52.074	0.000
PARITY1	1.929	2	0.965	5.996	0.003
LENGTH	79.155	1	79.155	492.024	0.000
Error	87.678	545	0.161		
Total	10684.926	550			
Corrected total	198.842	549			

[a] *R* squared = 0.559 (adjusted *R* squared = 0.556).

Custom Hypothesis Tests

Contrast Results (K matrix)

Parity re-coded (three levels) Polynomial contrast[a]			Dependent variable Weight (kg)
Linear	Contrast estimate		0.098
	Hypothesised value		0
	Difference (estimate − hypothesised)		0.098
	Std. error		0.030
	Sig.		0.001
	95% confidence interval	Lower bound	0.039
	for difference	Upper bound	0.157
Quadratic	Contrast estimate		−0.035
	Hypothesised value		0
	Difference (estimate − hypothesised)		−0.035
	Std. error		0.029
	Sig.		0.238
	95% confidence interval	Lower bound	−0.092
	For difference	Upper bound	0.023

[a] Metric = 1.000, 2.000, 3.000.

The Tests of Between-Subject Effects table shows that by adding a strong covariate, the explained variation has increased from 16.4% to 55.9% as indicated by the R square value. All three factors in the model are statistically significant but parity is now less significant at $P = 0.003$ compared to $P = 0.001$ in the former three-way ANOVA model. These P values, which are adjusted for the covariate, are more accurate than the P values from the previous one-way and three-way ANOVA models. The Contrast Results table shows that the linear trend for weight to increase with increasing parity remains significant, but slightly less so at $P = 0.001$.

Estimated Marginal Means

Estimates
Dependent Variable: Weight (kg)

			95% confidence interval	
Gender	Mean	Std. error	Lower bound	Upper bound
Male	4.494[a]	0.025	4.445	4.542
Femal	4.238[a]	0.025	4.190	4.287

[a] Covariates appearing in the model are evaluated at the following values: length (cm) = 54.841.

Pairwise Comparisons
Dependent Variable: Weight (kg)

		Mean difference			95% confidence interval for difference[a]	
(I) gender	(J) gender	(I − J)	Std. error	Sig.[a]	Lower bound	Upper bound
Male	Female	0.255*	0.035	0.000	0.186	0.325
Female	Male	−0.255*	0.035	0.000	−0.325	−0.186

Based on estimated marginal means.
*The mean difference is significant at the 0.05 level.
[a] Adjustment for multiple comparisons: least significant difference (equivalent to no adjustments).

Univariate Tests
Dependent Variable: Weight (kg)

	Sum of squares	*df*	Mean square	*F*	Sig.
Contrast	8.378	1	8.378	52.074	0.000
Error	87.678	545	0.161		

*The *F* tests the effect of gender. This test is based on the linearly independent pairwise comparisons among the estimated marginal means.

When there is a significant covariate in the model, the marginal means are calculated with the covariate held at its mean value. Thus, the marginal means are predicted means and not observed means. In this model, the marginal means are calculated at the mean value of the covariate length, that is 54.841 as shown in the footnote of the Estimates table. In this situation, the marginal means need to be treated with caution because they may not correspond with any situation in real life where the covariate is held at its mean value and is balanced between groups. In observational studies, the marginal means from such analyses often have no interpretation apart from group comparisons.

Testing the model assumptions

It is important to conduct tests to check that the assumptions of any ANOVA model have been met. By re-running the model with different options, statistics can be obtained to test that the residuals are normally distributed, that there are no influential multivariate outliers, that the variance is homogeneous and that there are no interactions between the covariate and the factors. Here, the assumptions are being tested only when final model is obtained but in practice the assumptions would be tested at each stage in the model building process. The SPSS commands shown in Box 5.9 can be used to test the model assumptions.

Box 5.9 SPSS commands for testing the model assumptions

SPSS Commands
weights – SPSS Data Editor
    Analyze → General Linear Model → Univariate
Univariate
    Click on Reset
    Highlight Weight and click into Dependent Variable
    Highlight Gender and Parity recoded (3 levels) and click into Fixed Factors
    Highlight Length, click into Covariate(s)
    Click on Model
Univariate: Model
    Click on Custom
    Under Build Term(s) pull down menu and click on Main effects
    Highlight gender, parity1 and length and click over into Model
    Pull down menu, click on All 2-way
    Highlight gender, parity1 and length, click over into Model
    Sum of squares: type III on pull down menu (default)
    Tick Include intercept in model (default), click Continue
Univariate
    Click on Save
Univariate: Save
    Under Predicted Values tick Unstandardized
    Under Residuals tick Standardized

Under Diagnostics tick Cook's distances and Leverage values
Click Continue
Univariate
Click on Options
Univariate Options
Tick on Estimates of effect size, Homogeneity tests, Spread vs level plot
Residual plot, and Lack of fit, click Continue
Univariate
Click OK

Univariate analysis of variance

Levene's Test of Equality of Error Variances[a]
Dependent Variable: Weight (kg)

F	*df1*	*df2*	Sig.
1.947	5	544	0.085

Tests the null hypothesis that the error variance of the dependent variable is equal across groups.
[a] Design:
Intercept+GENDER+PARITY1+LENGTH+GENDER * PARITY1+GENDER * LENGTH+PARITY1 * LENGTH

In Levene's Test of Equality of Error Variances table, Levene's test indicates that the differences in variances are not significantly different with a P value of 0.085. If the P value had been significant at < 0.05, regression would be the preferred method of analysis. Other options would be to halve the critical P values for any between-group differences say to $P = 0.025$ instead of $P = 0.05$. This is an arbitrary decision but would reduce the type I error rate. A less rigorous option would be to select a post-hoc test that adjusts for unequal variances.

Tests of Between-Subject Effects
Dependent Variable: Weight (kg)

Source	Type III sum of squares	*df*	Mean square	*F*	Sig.	Partial eta squared
Corrected model	114.742[a]	9	12.749	81.862	0.000	0.577
Intercept	18.697	1	18.697	120.056	0.000	0.182
GENDER	2.062	1	2.062	13.237	0.000	0.024
PARITY1	0.898	2	0.449	2.884	0.057	0.011
LENGTH	73.731	1	73.731	473.425	0.000	0.467
GENDER * PARITY1	0.230	2	0.115	0.739	0.478	0.003

Continued

	Type III sum					Partial eta
Source	**of squares**	***df***	**Mean square**	***F***	**Sig.**	**squared**
GENDER * LENGTH	2.434	1	2.434	15.631	0.000	0.028
PARITY1 * LENGTH	0.793	2	0.397	2.547	0.079	0.009
Error	84.099	540	0.156			
Total	10684.926	550				
Corrected total	198.842	549				

[a] *R* squared = 0.577 (adjusted *R* squared = 0.570).

The Sig. column in the Tests of Between-Subject Effects table shows that gender and length are significant predictors of weight with $P < 0.0001$ and that parity is a marginal predictor with $P = 0.057$. However, there is a significant interaction between gender and length at $P < 0.0001$ although there are no significant interactions between gender and parity ($P = 0.478$) or parity and length ($P = 0.079$).

When interactions are present in any multivariate model, the main effects of the variables involved in the interaction are no longer of interest because it is the interaction that describes the relationship between the variables and the outcome. However, the main effects must always be included in the model even though they are no longer of interest. The interaction between gender and length violates the ANCOVA model assumption that there is no interaction between the covariate and the factors. In this case, regression would be the preferred analysis. Alternatively, the ANCOVA could be conducted for males and females separately although this will reduce the precision around the estimates of effect simply because the sample size in each model is halved.

In the Tests of Between-Subject Effects table, an estimate of partial eta squared is reported for each effect. This statistic gives an estimate of the proportion of the variance that can be attributed to each factor. In ANCOVA, this statistic is calculated as the sum of squares for the effect divided by the sum of squares for the effect plus the sum of squares for the error. These partial eta squared values for each factor can be directly compared but cannot be added together to indicate how much of the variance of the outcome variable is accounted for by the explanatory variables.

Lack of Fit Tests
Dependent Variable: Weight (kg)

Source	Sum of squares	*df*	Mean square	*F*	Sig.	Partial eta squared
Lack of fit	20.907	114	0.183	1.236	0.070	0.249
Pure error	63.192	426	0.148			

The lack of fit test divides the total variance into the variance due to the interaction terms not included in the model (lack of fit) and the variance in the model (pure error). An F value that is not significant as in this table at $P = 0.070$ indicates that the model cannot be improved by adding further interaction terms, which in this case would have been the three-way interaction term between gender, parity and length. However, any significant interaction that includes the covariate would violate the assumption of the model.

It is important to examine the variance across the model using a spread-vs-level plot because the cell sizes in the model are unequal. The spread-vs-level plot shows one point for each cell. If the variance is not related to the cell means then unequal variances will not be a problem. However, if there is a relation such as the variance increasing with the mean of the cell, then unequal variances will bias the F value.

The Spread-vs-Level plot shown in Figure 5.7 indicates that the standard deviation on the y-axis increases with the mean weight of each gender and parity cell as shown on the x-axis. However, the range in standard deviations is relatively small, that is from approximately 0.45 to 0.65. This ratio of less than 1:2 for standard deviation, or 1:4 for variance, will not violate the ANOVA assumptions.

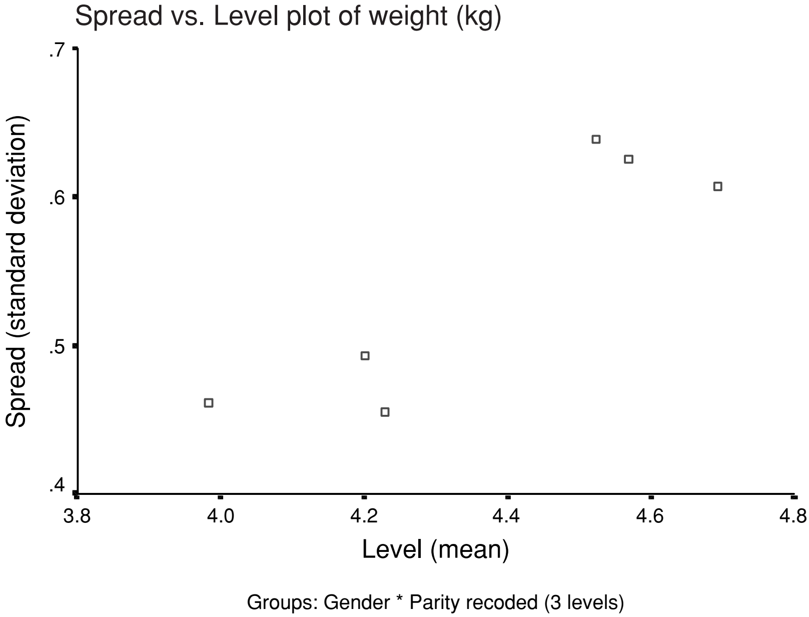

Figure 5.7 Spread (standard deviation) by level (mean) plot of weight for each gender and parity group.

If the variances are widely unequal, it is sometimes possible to reduce the differences by transforming the measurement. If there is a linear relation between the variance and the means of the cells and all the data values are positive, taking the square root or logarithm of the measurements may be helpful.

Transforming variables into units that are not easy to communicate are last resort methods to avoid violating the assumptions of ANOVA or ANCOVA. In practice, the use of a different statistical test such as multiple regression analysis may be preferable because the assumptions are not as restrictive.

Testing residuals: unbiased and normality

One assumption of ANOVA and ANCOVA is that the residuals are unbiased. This means that the differences between the observed and predicted values for each participant are not systematically different from one another. If the plot of the observed against predicted values, as shown in the centre of the top row, were funnel shaped or deviated markedly from the line of identity, which is a diagonal line across the plot, this assumption would be violated.

Using the commands in Box 5.9 the matrix plot shown in Figure 5.8 can be obtained. This plot shows that the observed and predicted values have a linear relationship with no systematic differences across the range. In addition, the negative and positive residuals balance one another with a random scatter around a horizontal centre line.

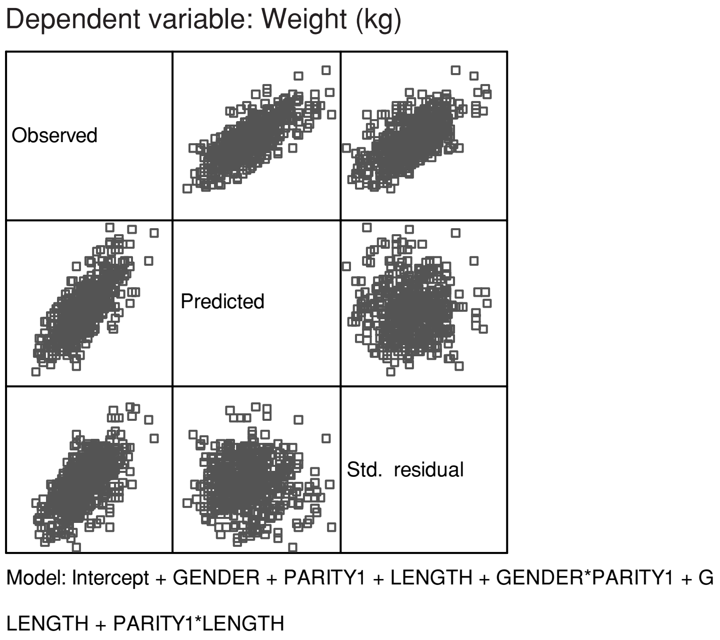

Figure 5.8 Matrix plot of observed and predicted values by standardised residuals for weight.

The assumption that the residuals, that is the within-group differences, have a normal distribution can be tested when running the ANOVA model. It is important that this assumption is met especially if the sample size is relatively small because the effect of non-normally distributed residuals or of multivariate outliers is to bias the P values.

When residuals are requested in *Save* as shown in Box 5.9, the residual for each case is created as a new variable at the end of the spreadsheet. Thus, the distribution of the residuals can be explored in more detail using standard tests of normality in *Analyze* → *Descriptive Statistics* → *Explore* as shown in Box 2.2 in Chapter 2, with the new variable Standardised Residual for weight as the dependent variable.

Descriptives

			Statistic	**Std. error**
Standardised residual for WEIGHT	Mean		0.0000	0.04229
	95% confidence interval for mean	Lower bound	−0.0831	
		Upper bound	0.0831	
	5% trimmed mean		0.0014	
	Median		−0.0295	
	Variance		0.984	
	Std. deviation		0.99177	
	Minimum		−2.69	
	Maximum		3.16	
	Range		5.85	
	Inter-quartile range		1.3246	
	Skewness		0.069	0.104
	Kurtosis		0.178	0.208

Extreme Values

			Case number	**Value**
Standardised residual for WEIGHT	Highest	1	256	3.16
		2	101	3.08
		3	404	3.03
		4	32	2.80
		5	447	2.73
	Lowest	1	252	−2.69
		2	437	−2.48
		3	311	−2.37
		4	35	−2.37
		5	546	−2.34

Tests of Normality

	Kolmogorov–Smirnov[a]			Shapiro-Wilk		
	Statistic	***df***	**Sig.**	**Statistic**	***df***	**Sig.**
Standardised residual for WEIGHT	0.020	550	0.200*	0.995	550	0.069

* This is a lower bound of the true significance.

[a] Lilliefors significance correction.

The descriptive statistics and the tests of normality show that the standardised residuals are normally distributed with a mean residual of zero and a standard deviation very close to unity at 0.992, as expected. The histogram and normal Q–Q plot shown in Figure 5.9 indicate only small deviations from normality in the tails of the distribution.

For an approximately normal distribution, 99% of standardised residuals will by definition fall within three standard deviations of the mean. Therefore, 1% of the sample is expected to be outside this range. In this sample size of 550 children, it would be expected that 1% of the sample, that is five children, would have a standardised residual outside the area that lies between -3 and $+3$ standard deviations from the mean. The Extreme Values table shows that residual scores for three children are more than 3 standard deviations from the mean and the largest standardised residual is 3.16. The number of outliers is less than would be expected by chance. In addition, all three outliers have values that are just outside the cut-off range and therefore are not of concern.

Identifying multivariate outliers: Leverage and discrepancy

To identify multivariate outliers, statistics such as leverage and discrepancy for each data point can be calculated. Leverage measures how far or remote a data point is from the remaining data but does not indicate whether the remote data point is on the same line as other cases or far away from the line. Thus, leverage does not provide information about the direction of the distance from the other data points[7]. Discrepancy indicates whether the remote data point is in line with other data points. Figure 5.10 shows how remote points or outliers can have a high leverage and/or a high discrepancy.

Cook's distances are a measure of influence, that is a product of leverage and discrepancy. Influence measures the change in regression coefficients (Chapter 6) if the data point is removed[6]. A recommended cut-off for detecting influential cases is a Cook's distance greater than $4/(n - k - 1)$, where n is the sample size and k is the number of explanatory variables in the model. In this example, any distance that is greater than $4/(550 - 3 - 1)$, or 0.007, should be investigated. Obviously the larger the sample size the smaller the cook's

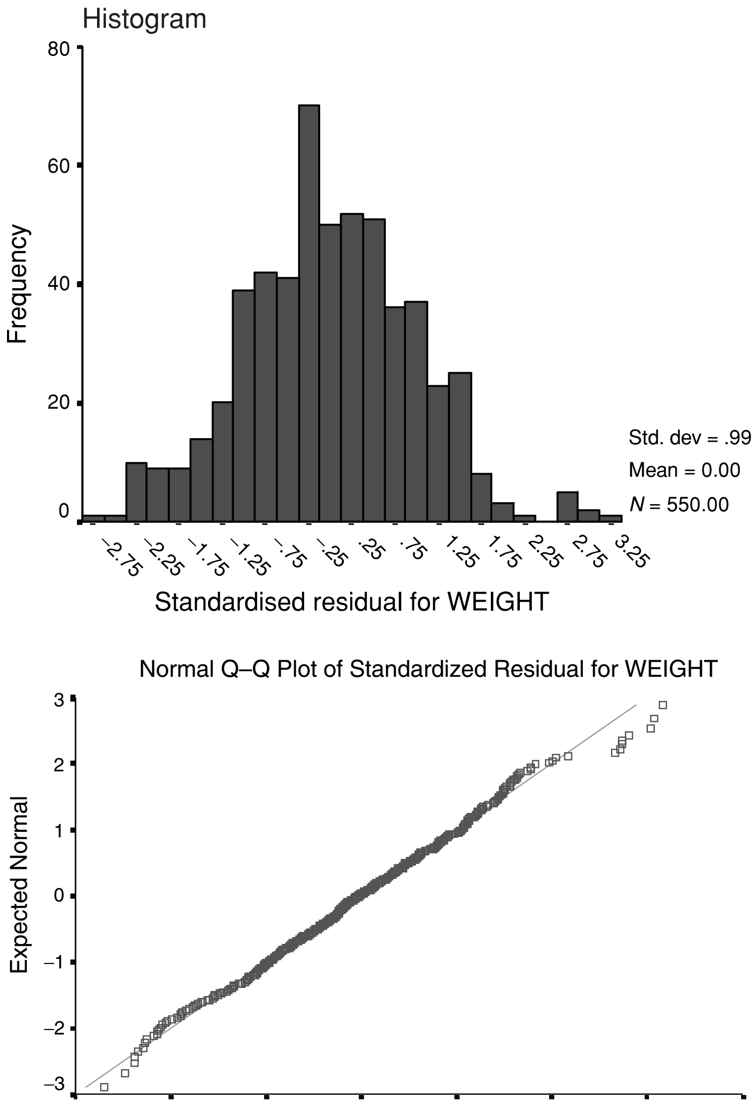

Figure 5.9 Plots of standardised residuals by weight.

distance becomes. Therefore in practice, Cook's distances above 1 should be investigated because these cases are regarded as influential cases or outliers.

A leverage value that is greater than $2(k + 1)/n$, where k is the number of explanatory variables in the model and n is the sample size, is of concern. In the working example, this value would be $2 \times (3 + 1)/550$, or 0.015. As with Cook's distance, this leverage calculation is also influenced by sample size

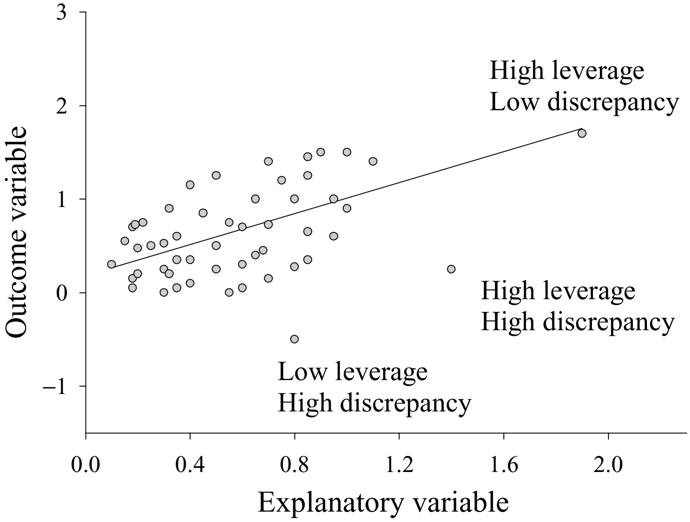

Figure 5.10 Distribution of data points and outliers.

and the number of explanatory variables in the model. In practice, leverage values less than 0.2 are acceptable and leverage values greater than 0.5 need to be investigated. Leverage is also related to Mahalanobis distance, which is another technique to identify multivariate outliers when regression is used[6] (Chapter 6).

Cook's distances can be plotted in a histogram using the SPSS commands shown Box 5.10. These commands can be repeated for leverage values.

Box 5.10 SPSS commands to examine potential multivariate outliers

SPSS Commands

weights – SPSS Data Editor

Graphs → Histogram

Histogram

Highlight Cook's distance for weight, click into Variable

Click OK

The plots shown in Figure 5.11 indicate that there are no multivariate outliers because there are no Cook's distances greater than 1 or leverage points greater than 0.2.

Deciding whether points are problematic will always be context specific and several factors need to be taken into account including sample size and diagnostic indicators. If problematic points are detected, it is reasonable to remove them, re-run the model and decide on an action depending on their influence on the results. Possible solutions are to re-code values to remove

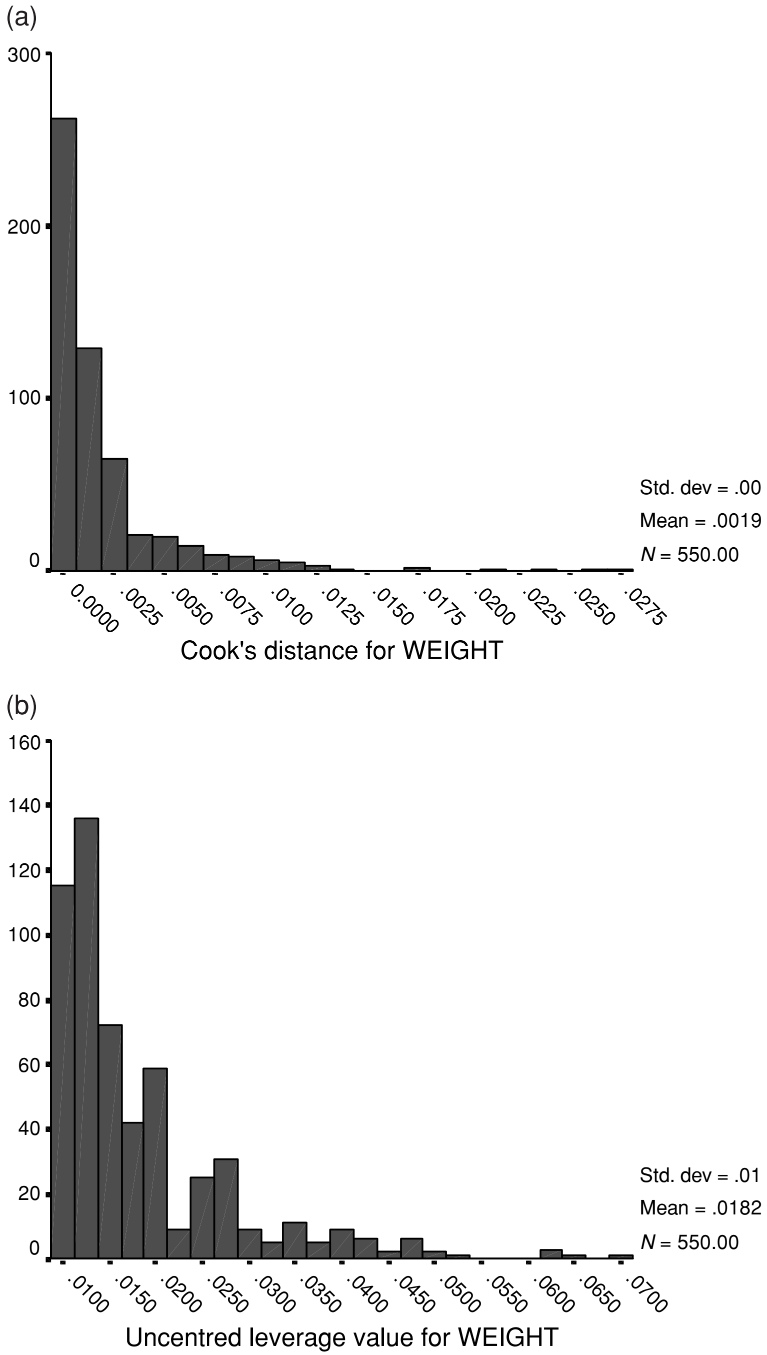

Figure 5.11 Histograms of Cook's distance and leverage values for weight.

their undue influence, to recruit a study sample with a larger sample size if the sample being tested is small or to limit the generalisability of the model.

Reporting the results

If the model assumptions had all been met, the results of the final ANCOVA model could be reported in a similar way to reporting the three-way ANOVA. The statistics reported should include information to assure readers that all ANCOVA assumptions had been met and should include values of partial eta squared to convey the relative contribution of each factor to the model. Other statistics to report are the total amount of variation explained and the significance of each factor in the model.

In the present ANCOVA model, because there was a significant interaction between factors, it is better to analyse the data using regression as described in Chapter 6.

Notes for critical appraisal

There are many assumptions for ANOVA and ANCOVA and it is important that all assumptions are tested and met to avoid inaccurate *P* values. Some of the most important questions to ask when critically appraising a journal article in which ANOVA or ANCOVA is used to analyse the data are shown in Box 5.11.

Box 5.11 Questions for critical appraisal

The following questions should be asked when appraising published results from analyses in which ANOVA or ANCOVA has been used:

- Have any repeated measures been treated as independent observations?
- Is the outcome variable normally distributed?
- Does each cell have an adequate number of participants?
- Are the variances between cells fairly similar?
- Are the residuals normally distributed?
- Are there any outliers that would tend to inflate or reduce differences between groups or that would distort the model and the standard errors, and therefore the *P* values?
- Does the model include any unreliable covariates or covariates that do not have a linear relationship with the outcome?
- If there is an increase in means across the range of a factor, has a trend test been used?
- Have tests of homogeneity and collinearity been included?
- Would regression have been a more appropriate statistical test to use?
- Do the *P* values reflect the differences between cell means and the group sizes?

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CHAPTER 6
Continuous data analyses: correlation and regression

Angling may be said to be so like mathematics that it can never be fully learnt.
IZAAK WALTON (1593–1683)

Objectives

The objectives of this chapter are to explain how to:
- explore a linear relation between two continuous variables
- interpret parametric and non-parametric correlation coefficients
- build a regression model that conforms to satisfies assumptions of regression assumptions
- use a regression model as a predictive equation
- include binary and dummy group variables in a multivariate model
- plot regression equations that include binary group variables
- include more than one continuous variable in a multivariate model
- test for collinearity and interactions
- identify and deal with outliers and remote points
- explore non-linear fits for regression models
- critically appraise the literature when regression models are reported

Correlation coefficients

A correlation coefficient describes how closely two variables are related, that is the amount of variability in one measurement that is explained by another measurement. The range of a correlation coefficient is from −1 to +1, where +1 and −1 indicate that one variable has a perfect linear association with the other variable and that both variables are measuring the same entity without error. In practice, this rarely occurs because even if two instruments are intended to measure the same entity both usually have some degree of measurement error.

A correlation coefficient of zero indicates a random relationship and the absence of a linear association. A positive coefficient value indicates that both variables increase in value together and a negative coefficient value indicates that one variable decreases in value as the other variable increases. It is important to note that a significant association between two variables does not imply that they have a causal relationship. Also, a correlation coefficient that is not significant does not imply that there is no relationship between the variables because there may be a non-linear relationship such as a curvilinear or cyclical relationship.

Correlation coefficients are rarely used as important statistics in their own right. An inherent limitation is that correlation coefficients reduce complex relationships to a single number that does not adequately explain the relationship between the two variables. Another inherent problem is that the statistical significance of the test is often over-interpreted. The P value is an estimate of whether the correlation coefficient is significantly different from zero so that a small correlation of no clinical importance can become statistically significant, especially when the sample size is large. In addition, the range of the data as well as the relationship between the two variables influences the correlation coefficient.

There are three types of bivariate correlations and the type of correlation that is used to examine a linear relation is determined by the nature of the variables.

Pearson's correlation coefficient (r) is a parametric correlation coefficient that is used to measure the association between two continuous variables that are both normally distributed. The correlation coefficient (r) can be squared to give the coefficient of determination (r^2), which is an estimate of the per cent of variation in one variable that is explained by the other variable.

The assumptions for using Pearson's correlation coefficient are shown in Box 6.1.

Box 6.1 Assumptions for using Pearson's correlation coefficient

The assumptions that must be satisfied to use Pearson's correlation coefficient are:

- both variables must be normally distributed
- the sample must have been selected randomly from the general population
- the observations are independent of one another
- the relation between the two variables is linear
- the variance is constant over the length of the data

If the assumption of random selection is not met, the correlation coefficient does not describe the true association between two variables that would be found in the general population. In this case, it would not be valid to generalise the association to other populations or to compare the r value with results from other studies.

Spearman's ρ (rho) is a rank correlation coefficient that is used for two ordinal variables or when one variable has a continuous normal distribution and the other variable is categorical or non-normally distributed. When this statistic is computed, the categorical or non-normally distributed variable is ranked, that is sorted into ascending order and numbered sequentially, and then a correlation of the ranks with the continuous variable that is equivalent to Pearson's r is calculated.

Kendall's τ (*tau*) is used for correlations between two categorical or non-normally distributed variables. In this test, Kendall's τ is calculated as the number of concordant pairs minus the number of disconcordant pairs divided by the total number of pairs. Kendall's tau-b is adjusted for the number of pairs that are tied.

Research question

The spreadsheet **weights.sav**, which was used in Chapter 5, contains the data from a population sample of 550 term babies who had their weight recorded at 1 month of age.

Question:	Is there an association between the weight, length and head circumference of 1 month old babies?
Null hypothesis:	That there is no association between weight, length and head circumference of babies at 1 month of age.
Variables:	Weight, length and head circumference (continuous)

All three variables of weight, length and head circumference are continuous variables that have a normal distribution and therefore their relationships to one another can be examined using Pearson's correlation coefficients. Before computing any correlation coefficient, it is important to obtain scatter plots to obtain an understanding of the nature of the relationships between the variables. Box 6.2 shows the SPSS commands to obtain the scatter plots.

Box 6.2 SPSS commands to obtain scatter plots between variables

SPSS Commands

weights – SPSS Data Editor
    Graphs → Scatter
Scatterplot
    Click on Matrix and click on Define
Scatterplot Matrix
    Highlight Weight, Length, Head circumference, click over into Matrix Variables
    Click OK

The matrix in Figure 6.1 shows each of the variables plotted against one another. The number of rows and columns is equal to the number of variables selected. Each variable is shown once on the x-axis and once on the y-axis to give six plots, three of which are mirror images of the other three. In Figure 6.1, the scatter plot between weight and length is shown in the middle box on the top row, the scatter plot between weight and head circumference is in the right hand box on the top row, and the scatter plot between length and head

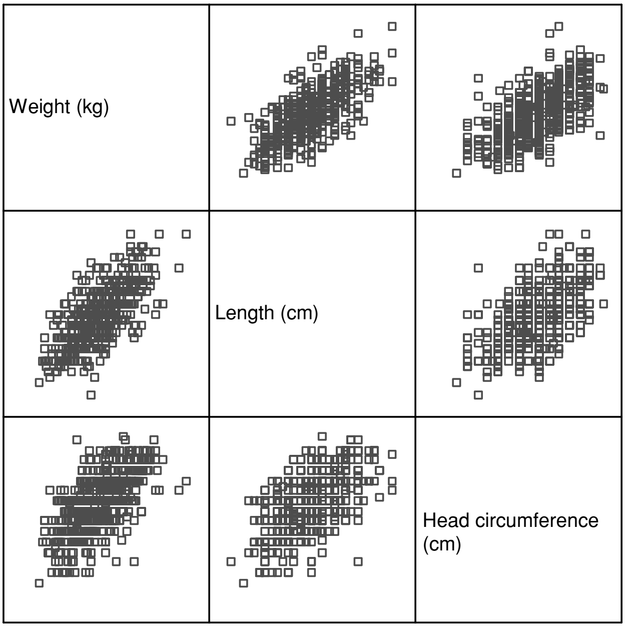

Figure 6.1 Scatter plot of weight by length by head circumference.

circumference is in the third column of the middle row. All scatter plots in Figure 6.1 slope upwards to the right indicating a positive association between the two variables. If an association was negative, the scatter plot would slope downwards to the right.

The plots shown in Figure 6.1 indicate that there is a reasonable, positive linear association for all bivariate combinations of the three variables. It is clear that weight has a closer relationship with length than with head circumference in that the scatter around the plot is narrower. Box 6.3 shows the SPSS commands to obtain the correlation coefficients between the three variables. Normally only one type of coefficient would be requested but to illustrate the difference between coefficients, all three are requested in this example.

Box 6.3 SPSS commands to obtain correlation coefficients

SPSS Commands
weights – SPSS Data Editor
    Analyze → Correlate → Bivariate
Bivariate Correlations
    Highlight Weight, Length, Head circumference, click over into Variables
    Under Correlation Coefficients, tick Pearson (default), Kendall's tau-b and Spearman
    Under Test of Significance, tick Two-Tailed (default)
    Click OK

Correlations

Correlations

		Weight (kg)	Length (cm)	Head circumference (cm)
Weight (kg)	Pearson correlation	1	0.713**	0.622**
	Sig. (two-tailed)	.	0.000	0.000
	N	550	550	550
Length (cm)	Pearson correlation	0.713**	1	0.598**
	Sig. (two-tailed)	0.000	.	0.000
	N	550	550	550
Head circumference (cm)	Pearson correlation	0.622**	0.598**	1
	Sig. (two-tailed)	0.000	0.000	.
	N	550	550	550

** Correlation is significant at the 0.01 level (two-tailed).

A comparison of the Pearson correlations (*r* values) in the Correlations table shows that the best predictor of weight is length with an *r* value of 0.713 compared to a weaker, but moderate association between weight and head circumference with an *r* value of 0.622. Head circumference is related to length with a slightly lower *r* value of 0.598. Despite their differences in magnitude, the correlation coefficients are all highly significant at the $P <$ 0.0001 level emphasising the insensitive nature of the *P* values for selecting the most important predictors of weight.

Non-parametric Correlations

Correlations

			Weight (kg)	Length (cm)	Head circumference (cm)
Kendall's tau_b	Weight (kg)	Correlation coefficient	1.000	0.540**	0.468**
		Sig. (two-tailed)	.	0.000	0.000
		N	550	550	550
	Length (cm)	Correlation coefficient	0.540**	1.000	0.454**
		Sig. (two-tailed)	0.000	.	0.000
		N	550	550	550
	Head circumference (cm)	Correlation coefficient	0.468**	0.454**	1.000
		Sig. (two-tailed)	0.000	0.000	.
		N	550	550	550

Continued

			Weight (kg)	Length (cm)	Head circumference (cm)
Spearman's rho	Weight (kg)	Correlation coefficient	1.000	0.711**	0.626**
		Sig. (two-tailed)	.	0.000	0.000
		N	550	550	550
	Length (cm)	Correlation coefficient	0.711**	1.000	0.596**
		Sig. (two-tailed)	0.000	.	0.000
		N	550	550	550
	Head circumference (cm)	Correlation coefficient	0.626**	0.596**	1.000
		Sig. (two-tailed)	0.000	0.000	.
		N	550	550	550

** Correlation is significant at the 0.01 level (two-tailed).

In the Non-parametric Correlations table, Kendall's tau-b coefficients are all lower than the Pearson's coefficients in the previous table but Spearman's coefficients are similar in magnitude to Pearson's coefficients.

The influence on *r* values when using a selected sample rather than a random sample can be demonstrated by repeating the analysis using only part of the data set. Using *Analyze →Descriptive Statistics →Descriptives* shows that length ranges from a minimum value of 48.0 cm to a maximum value of 62.0 cm. To examine the correlation in a selected sample, the data set can be restricted to babies less than 55.0 cm in length using the commands shown in Box 6.4.

Box 6.4 SPSS commands to calculate a correlation coefficient for a subset of the data

SPSS Commands

weights – SPSS Data Editor
    Data → Select Cases
Select Cases
    Tick 'If condition is satisfied' → Click on 'If' box
Select Cases: If
    Highlight Length and click over into white box
    Type in '<55' following length
    Click Continue
Select Cases
    Click OK

When *Select Cases* is used, the line numbers of cases that are unselected appear in Data View with a diagonal line through them indicating that they will be excluded from any analysis. In addition, a filter variable to indicate the status of each case in the analysis is generated at the end of the spreadsheet and the text *Filter On* is shown in the bottom right hand side of the Data View screen.

To examine the relationship between the variables for only babies less than 55.0 cm in length, Pearson's correlation coefficients can be obtained using the commands shown in Box 6.2.

Correlations

Correlations

		Weight (kg)	**Length (cm)**	**Head circumference (cm)**
Weight (kg)	Pearson correlation	1	0.494**	0.504**
	Sig. (two-tailed)	.	0.000	0.000
	N	272	272	272
Length (cm)	Pearson correlation	0.494**	1	0.390**
	Sig. (two-tailed)	0.000	.	0.000
	N	272	272	272
Head circumference (cm)	Pearson correlation	0.504**	0.390**	1
	Sig. (two-tailed)	0.000	0.000	.
	N	272	272	272

** Correlation is significant at the 0.01 level (two-tailed).

When compared with Pearson's *r* values from the full data set, the correlation coefficient between weight and length is substantially reduced from 0.713 to 0.494 when the upper limit of length is reduced from 62 cm to 55 cm. However, the top centre plot in Figure 6.1 shows that the relationship between weight and length in the lower half of the data is similar to the total sample. In general, *r* values are higher when the range of the explanatory variable is wider even though the relationship between the variables is the same. For this reason, only the coefficients from random population samples have an unbiased value and can be compared with one another.

Once the correlation coefficients are obtained, the full data set can be reselected using the command sequence *Data → Select Cases → All cases.*

Regression models

Regression models are used to measure the extent to which one or more explanatory variables predict an outcome variable. In this, a regression model is used to fit a straight line through the data, where the regression line is the best predictor of the outcome variable using one or more explanatory variables.

There are two principal purposes for building a regression model. The most common purpose is to build a predictive model, for example in situations in which age and gender are used to predict normal values in lung size or body mass index (BMI). Normal values are the range of values that occur naturally in the general population. In developing a model to predict normal values, the emphasis is on building an accurate predictive model.

The second purpose of using a regression model is to examine the effect of an explanatory variable on an outcome variable after adjusting for other important explanatory factors. These types of models are used for hypothesis testing. For example, a regression model could be built using age and gender to predict BMI and could then be used to test the hypothesis that groups with different exercise regimes have different BMI values.

The mathematics of regression are identical to the mathematics of analysis of covariance (ANCOVA). However, regression provides more information than ANCOVA in that a linear equation is generated that explains the relationship between the explanatory variables and the outcome. By using regression, more information about the relationships between variables and the between-group differences is obtained. Regression can also be a more flexible approach because some of the assumptions such as those relating to cell and variance ratios are not as restrictive as the assumptions for ANCOVA. However, in common with ANCOVA, it is important to remember that regression gives a measure of association at one point in time only, that is, at the time the measurements were collected, and a significant association does not infer causality.

Although the mathematics of regression are similar to ANOVA in that the explained and unexplained variations are compared, some terms are labelled differently. In regression, the distance between an observed value and the overall mean is partitioned into two components – the variation about the regression, which is also called the residual variation, and the variation due to the regression[1]. Figure 6.2 shows how the variation for one data point, shown as a circle, is calculated.

The variation about the regression is the explained variation and the variation due to the regression is the unexplained variation. As in ANOVA, these distances are squared and summed and the mean square is calculated. The F value, which is calculated as the regression mean square divided by the residual mean square, ranges from 1 to a large number. If the two sources of variance are similar, there is no association between the variables and the F value is close to 1. If the variation due to the regression is large compared to the variation about the regression, then the F value will be large indicating a strong association between the outcome and explanatory variables.

When there is only one explanatory variable, the equation of the best fit for the regression line is as follows:

$$y = a + bx$$

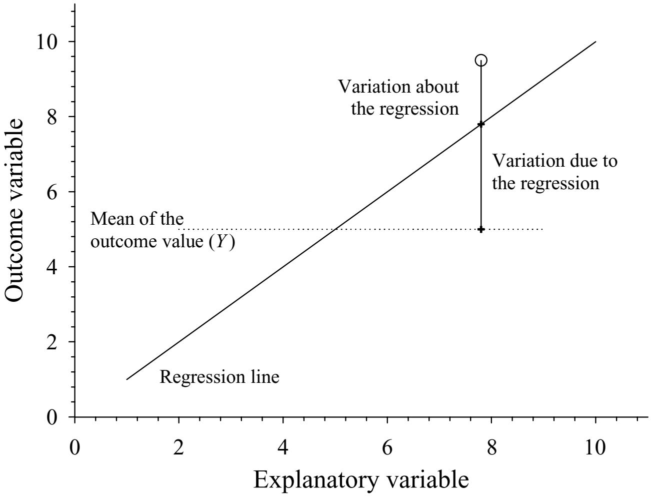

Figure 6.2 Calculation of the variation in regression.

where '*y*' is the value of the outcome variable, '*x*' is the value of the explanatory variable, '*a*' is the intercept of the regression line and '*b*' is the slope of the regression line. When there is only one explanatory variable, this is called a simple linear regression.

In practice, the slope of the line, as estimated by '*b*', represents the unit change in the outcome variable '*y*' with each unit change in the explanatory variable '*x*'. If the slope is positive, '*y*' increases as '*x*' increases and if the slope is negative, '*y*' decreases as '*x*' increases. The intercept is the point at which the regression line intersects with the *y*-axis when the value of '*x*' is zero. This value is part of the regression equation but does not usually have any clinical meaning. The fitted regression line passes through the mean values of both the explanatory variable '*x*' and the outcome variable '*y*'.

When using regression, the research question must be framed so that the explanatory and outcome variables are classified correctly. An important concept is that regression predicts the mean y value given the observed x value and the error around the explanatory variable is not taken into account. Therefore, measurements that can be taken accurately, such as age and height, make good explanatory variables. Measurements that are difficult to measure accurately or are subject to bias, such as birth weight recalled by parents when the baby has reached school age, should be avoided as explanatory variables.

Assumptions for regression

To avoid bias in a regression model or a lack of precision around the estimates, the assumptions for using regression that are shown in Box 6.5 must be tested and met. In regression, mean values are not compared as in ANOVA so that any bias between groups as a result of non-normal distributions is not as problematic. Regression models are robust to moderate degrees of non-normality provided that the sample size is large and that there are few multivariate outliers in the final model. In general, the residuals but not the outcome variable has to be normally distributed. Also, the sample does not have to be selected randomly because the regression equation describes the relation between the variables and is not influenced by the spread of the data. However, it is important that the final prediction equation is only applied to populations with the same characteristics as the study sample.

Box 6.5 Assumptions for using regression

The assumptions that must be met when using regression are as follows:

Study design

- the sample is representative of the population to which inference will be made
- the sample size is sufficient to support the model
- the data have been collected in a period when the relationship between the outcome and the explanatory variable/s remains constant
- all important explanatory variables (covariates) are included

Independence

- all observations are independent of one another
- there is low collinearity between explanatory variables

Model building

- the relation between the explanatory variable/s and the outcome variable is approximately linear
- the explanatory variables correlate with the outcome variable
- the residuals are normally distributed
- the variance is homoscedastic, that is constant over the length of the model
- there are no multivariate outliers that bias the regression estimates

Under the study design assumptions shown in Box 6.5, the assumption that the data are collected in a period when the relationship remains constant is important. For example, in building a model to predict normal values for blood pressure the data must be collected when the participants have been resting rather than exercising and participants taking anti-hypertensive medications should be excluded. It is also important that all known covariates are included in the model before testing the effects of new variables added to the model.

The two assumptions of independence between observations and explanatory variables are important. When explanatory variables are significantly related to each other, a decision needs to be made about which variable to include and which variable to exclude.

The remaining assumptions about the nature of the data can be tested when building the model. In this chapter, the assumptions are tested after obtaining a parsimonious model but in practice the assumptions should be tested at each step in the model building process.

Research question

Using the spreadsheet **weights.sav,** regression analysis can be used to answer the following research question:

Question:	Can body length be used to predict weight at 1 month of age?
Null hypothesis:	That there is no relation between length and weight at 1 month.
Variables:	Outcome variable = weight (continuous) Explanatory variable = length (continuous)

The SPSS commands to obtain a regression equation for the relation between length and weight are shown in Box 6.6.

Box 6.6 SPSS commands to obtain regression estimates

SPSS Commands

```
weights – SPSS Data Editor
        Analyze → Regression → Linear
Linear Regression
        Highlight Weight, click into Dependent box
        Highlight Length, click into Independent(s) box
        Method = Enter (default)
        Click OK
```

Regression

Model Summary

Model	*R*	*R* square	Adjusted *R* square	Std. error of the estimate
1	0.713[a]	0.509	0.508	0.42229

[a] Predictors: (constant), length (cm).

ANOVA[b]

Model		Sum of squares	*df*	Mean square	*F*	Sig.
1	Regression	101.119	1	101.119	567.043	0.000[a]
	Residual	97.723	548	0.178		
	Total	198.842	549			

[a] Predictors: (constant), length (cm).

[b] Dependent variable: weight (kg).

In linear regression, the R value in the Model Summary table is the multiple correlation coefficient and is the correlation between the observed and predicted values of the outcome variable. The value of R will range between 0 and 1. R can be interpreted in a similar way to Pearson's correlation coefficient. In simple linear regression, R is the absolute value of Pearson's correlation coefficient between the outcome and explanatory variable.

The R square value is the square of the R value, that is 0.713×0.713, and is often called the coefficient of determination. R square has a valuable interpretation in that it indicates the per cent of the variance in the outcome variable that can be explained or accounted for by the explanatory variables. The R square value of 0.509 indicates a modest relationship in that 50.9% of the variation in weight is explained by length. The adjusted R square value is the R value adjusted for the number of explanatory variables included in the model and can therefore be compared between models that include different numbers of explanatory variables. The standard error of the estimate of 0.42229 is the standard error around the outcome variable weight at the mean value of the explanatory variable length and as such gives an indication of the precision of the model.

In the ANOVA table, the F value is calculated as the unexplained variation due to the regression divided by the explained variation about the regression, or the residual variation. Thus, F is the regression mean square of 101.119 divided by the residual mean square of 0.178, or 568.08. The resulting F value of 567.043 in the table is slightly different as a result of rounding errors and is highly significant at $P < 0.0001$ indicating that there is a significant linear relation between length and weight.

Coefficients[a]

		Unstandardised coefficients		Standardised coefficients		
Model		*B*	Std. error	Beta	*t*	Sig.
1	(Constant)	−5.412	0.411		−13.167	0.000
	Length (cm)	0.178	0.007	0.713	23.813	0.000

[a] Dependent variable: weight (kg).

The Coefficients table shows the unstandardised coefficients that are used to formulate the regression equation in the form of $y = a + bx$ as follows:

$$\text{Weight} = -5.412 + (0.178 \times \text{Length})$$

Because length is the only explanatory variable in the model, the standardised coefficient, which indicates the relative contribution of a variable to the model, is the same as the R value shown in the first table. The t values, which are calculated by dividing the beta values (unstandardised coefficient B) by their standard errors, are a test of whether each regression coefficient is significantly different from zero. In this example, both the constant (intercept) and slope of the regression line are significantly different from zero at $P < 0.0001$ which is shown in the column labelled 'sig'. For length, the square of the t value is equal to the F value in the ANOVA table, that is the square of 23.813 is equal to 567.043.

Regression equations can only be generalised to samples with the same characteristics as the study sample. Thus, this regression model only describes the relation between weight and length in 1 month old babies who were term births because premature birth was an exclusion criterion for study entry. The model could not be used to predict normal population values because they are not from a random population sample, which would include premature births. However, the model could be used to predict normal values for term babies.

Plotting the regression

The commands shown in Box 6.7 can be used to obtain a scatter plot, plot the observed values of weight against length and to draw the regression line with prediction intervals.

Box 6.7 SPSS commands to obtain a scatter plot

SPSS Commands

weights – SPSS Data Editor

Graphs → Interactive → Scatterplot

Create Scatterplot

Highlight Length, hold left hand mouse button and drag into x-axis box
Highlight Weight, hold left hand mouse button and drag into y-axis box
Click on Fit
Pull down menu under Method and highlight Regression
Prediction Lines: tick Mean and Individual
Click OK

In Figure 6.3, the 95% mean prediction interval around the regression line is a 95% confidence interval, that is the area in which there is 95% certainty that

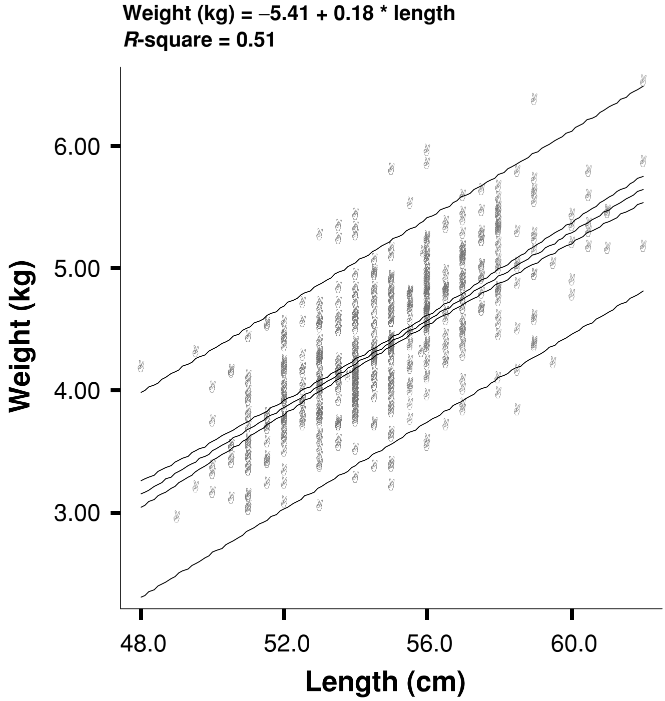

Figure 6.3 Scatter plot of weight on length with regression line and 95% confidence interval.

the true regression line lies. This interval band is slightly curved because the errors in estimating the intercept and the slope are included in addition to the error in predicting the outcome variable[2]. The error in estimating the slope increases as the difference between the predicted value and the actual value of the explanatory variable increases, resulting in a curved 95% confidence band around the sample regression line. In Figure 6.3, the 95% confidence interval is narrow as a result of the large sample size.

The 95% individual prediction interval is the larger band around the regression line in Figure 6.3. This interval in which 95% of the data points lie is the distance between the 2.5 and 97.5 percentiles. This interval is used to predict normal values. Clearly, any definition of normality is specific to the context but normal values should only be based on large sample sizes, preferably of at least 200 participants[3].

Multiple linear regression

A regression model in which the outcome variable is predicted from two or more explanatory variables is called a multiple linear regression. Explanatory variables may be continuous or categorical. For example, it is common to use height and age, both of which are continuous variables, to predict lung size or to use age and gender, a continuous and a categorical variable, to predict BMI. For multiple regression, the equation that explains the line of best fit, i.e. the regression line, is

$$y = a + b_1x_1 + b_2x_2 + b_3x_3 + \cdots$$

where 'a' is the intercept and 'b_i' is slope for each explanatory variable. In effect, b_1,b_2,b_3, etc. are the weights assigned to each of the explanatory variables in the model. In multiple regression models, the coefficient for a variable can be interpreted as the unit change in the outcome variable with each unit change in the explanatory variable when all of the other explanatory variables are held constant.

Multiple regression is used when there are several explanatory variables that predict an outcome or when the effect of a factor that can be manipulated is being tested. For example, height, age and gender could be used to predict lung function and then the effects of other potential explanatory variables such as current respiratory symptoms or smoking history could be tested. In multiple regression models, all explanatory variables that have an important association with the outcome should be included.

Multiple linear regression models should be built up gradually through a series of univariate bivariate, and multivariate methods. In multiple regression, each explanatory variable should ideally have a significant correlation with the outcome variable but the explanatory variables should not be significantly correlated with one another, that is collinear. Models should not be over-fitted with a large number of variables that increase the *R* square by small amounts. In over-fitted models, the *R* square may decrease when the model is applied to other data.

Decisions about which variables to remove or include in a model should be based on expert knowledge and biological plausibility in addition to statistical considerations. These decisions often need to take cost, measurement error and theoretical constructs into account in addition to the strength of association indicated by *R* values, *P* values and standardised coefficients. The ideal model should be parsimonious, that is comprising of the smallest number of variables that predict the largest amount of variation.

Once a decision has been made about which explanatory variables to test in a model, the distribution of both the outcome and the continuous explanatory variables should be examined using methods outlined in Chapter 2, largely to identify any univariate outliers. Also, the order in which the explanatory variables are entered into the model is important because this can make a difference to the amount of variance that is explained by each explanatory variable, especially when explanatory variables are significantly related to each other[4].

There are three different methods of entering the explanatory variables that is standard, stepwise or sequential[5]. In standard multiple regression, called the enter method in SPSS, all variables are entered into the model together and the unique contribution of each variable to the outcome variable is calculated. However, an explanatory variable that is correlated with the outcome variable may not be a significant predictor when the other explanatory variables have accounted for a large proportion of the variance so that the remaining variance is small[5].

In stepwise multiple regression, the order of the explanatory variables is determined by the strength of their correlation with the outcome variable or by predetermined statistical criteria. The stepwise procedure can be forward selection, backward deletion or stepwise, all of which are available options in SPSS. In forward selection, variables are added one at a time until the addition of another variable accounts only for a small amount of variance. In backward selection, all variables are entered and then are deleted one at a time if they do not contribute significantly to the prediction of the outcome. Forward selection and backward deletion may not result in the same regression equation[2]. Stepwise is a combination of both forward selection and backward deletion in which variables are added one at a time and retained if they satisfy set statistical criteria but are deleted if they no longer contribute significantly to the model[5].

In sequential multiple regression, which is also called hierarchical regression, the order of entering the explanatory variables is determined by the researcher using logical or theoretical factors, or by the strength of the correlation with the outcome variable. When each new variable is entered, the variance contributed by the variable, possible collinearity with other variables and the influence of the variable on the model are assessed. Variables can be entered one at a time or together in blocks and the significance of each variable, or each variable in the block, is assessed at each step. This method delivers a stable and reliable model and provides invaluable information about the inter-relationships between the explanatory variables.

Sample size considerations

For multiple regression, it is important to have an adequate sample size. A simple rule that has been suggested for predictive equations is that the minimum number of cases should be at least 100 or, for stepwise regression, that the number of cases should be at least $40 \times m$, where m is the number of variables in the model[5]. More precise methods for calculating sample size and power are available[6]. To avoid underestimating the sample size for regression, sample size calculations should be based on the regression model itself and not on correlation coefficients.

It is important not to include too many explanatory variables in the model relative to the number of cases because this can inflate the R^2 value. When the sample size is very small, the R^2 value will be artificially inflated, the adjusted R^2 value will be reduced and the imprecise regression estimates may have no sensible interpretation. If the sample size is too small to support the number of explanatory variables being tested, the variables can be tested one at a time and only the most significant included in the final model. Alternatively, a new explanatory variable can be created that is a composite of the original variables, for example BMI could be included instead of weight and height.

A larger sample size increases the precision around the estimates by reducing standard errors and often increases the generalisability of the results. The sample size needs to be increased if a small effect size is anticipated or if there is substantial measurement error in any variable, which tends to reduce statistical power to demonstrate significant associations between variables.

It is important to achieve a balance in the regression model with the number of explanatory variables and sample size, because even a small *R* value will become statistically significant when the sample size is very large. Thus, when the sample size is large it is prudent to be cautious about type I errors. When the final model is obtained, the clinical importance of estimates of effect size should be used to interpret the coefficients for each variable rather than reliance on *P* values.

Collinearity

Collinearity is a term that is used when two or more of the explanatory variables are significantly related to one another. The issue of collinearity is only important for the relationships between explanatory variables and naturally does not need to be considered in relationships between the explanatory variables and the outcome.

Regression is more robust to some degrees of collinearity than ANOVA but the smaller the sample size and the larger the number of variables in the model, the more problematic collinearity becomes. Important degrees of collinearity need to be reconciled because they can distort the regression coefficients and lead to a loss of precision, that is inflated standard errors of the beta coefficients, and thus to an unstable and unreliable model. In extreme cases of collinearity, the direction of effect, that is the sign, of a regression coefficient may change.

Correlations between explanatory variables cause logical as well as statistical problems. If one variable accounts for most of the variation in another explanatory variable, the logic of including both explanatory variables in the model needs to be considered since they are approximate measures of the same entity. The correlation (r) between explanatory variables in a regression model should not be greater than 0.70.[7] For this reason, the decision of which variables to include should be based on theoretical constructs rather than statistical considerations based on regression estimates. Variables that can be measured with reliability and with minimum measurement error are preferred whereas measurements that are costly, invasive, unreliable or removed from the main causal pathway are less useful in predictive models.

The amount of collinearity in a model is estimated by the variance inflation factor (VIF), which is calculated as $1/(1 - R^2)$ where R^2 is the squared multiple correlation coefficient. In essence, VIF measures how much the variance of the regression coefficient has been inflated due to collinearity with other explanatory variables[8]. In regression models, *P* values rely on an estimate of variance around the regression coefficients, which is proportional to the VIF and thus if the VIF is inflated, the P value may be unreliable. A VIF that is large, say greater than or equal to 4, is a sign of collinearity and the regression coefficients, their variances and their P values are likely to be unreliable.

In SPSS, collinearity is estimated by tolerance, that is $1 - R^2$. Tolerance has an inverse relationship to VIF in that VIF = 1/tolerance. Tolerance values close to zero indicate collinearity[8]. In regression, tolerance values less than 0.2 are usually considered to indicate collinearity. The relation between R, tolerance and VIF is shown in Table 6.1. A tolerance value below 0.5, which corresponds with an R value above 0.7 is of concern.

Table 6.1 Relation between *R*, tolerance and variance inflation factor (VIF)

R	Tolerance	VIF
0.25	0.94	1.07
0.50	0.75	1.33
0.70	0.51	1.96
0.90	0.19	5.26
0.95	0.10	10.26

Collinearity can be estimated from examining the standard errors and from tolerance values as described in the examples below, or collinearity statistics can be obtained in the *Statistics* options under the *Analyze →Regression→ Linear* commands.

Multiple linear regression: testing for group differences

Regression can be used to test whether the relation between the outcome and explanatory variables is the same across categorical groups, say males and females. Rather than split the data set and analyse the data from males and females separately, it is often more useful to incorporate gender as a binary explanatory variable in the regression model. This process maintains statistical power by maintaining sample size and has the advantage of providing an estimate of the size of the difference between the gender groups.

The spreadsheet **weights.sav** used previously in this chapter will be used to answer the following research questions.

Research question

Question: Is the prediction equation of weight using length different for males and females or for babies with siblings?

Variables: Outcome variable = weight (continuous)
Explanatory variables = length (continuous), gender (category, two levels) and parity (category, two levels)

In this model, length is included because it is an important predictor of weight. In effect, the regression model is used to adjust weight for differences in length between babies and then to test the null hypothesis that there is no difference in weight between groups defined by gender and parity.

It is simple to include a categorical variable in a regression model when the variable is binary, that is, has two levels only. Binary regression coefficients have a straight forward interpretation if the variable is coded 0 for the comparison group, for example a factor that is absent or reply of no, and 1 for the group of interest, for example a factor that is present or a reply that is coded yes. The *Transform → Recode* commands shown in Box 1.10 in Chapter 1 can be used to re-code gender into a new variable labelled gender2 with values 0 and 1, making an arbitrary decision to code male gender as the comparison group. Similarly, parity can be re-coded into a new variable, parity2 with the value 0 for singletons unchanged and with values of 1 or greater re-coded to 1 using the *Range* option from *1 through 3*. Once re-coded, values and labels for both variables need to be added in the Variable View screen and the numbers in each group verified as correct using the frequency commands shown in Box 1.7 in Chapter 1. It is important to always have systems in place to check for possible re-coding errors and to document re-coded group numbers in any new variables.

In this chapter, regression equations are built using the sequential method. To add variables to the regression model in blocks, the commands shown in Box 6.8 can be used with the enter method and block option. Prior bivariate analysis using t-tests for gender and one-way ANOVA for parity (not shown) indicated that the association between gender and weight is stronger than the association between parity and weight. Therefore, gender is added in the model before parity. Using the sequential method, the statistics of the two models are easily compared, collinearity between variables can be identified and reasons for any inflation in standard errors and loss of precision become clear.

Box 6.8 SPSS commands to generate a regression model with a binary explanatory variable

SPSS Commands

weights – SPSS Data Editor

Analyze → Regression → Linear

Linear Regression

Highlight Weight, click into Dependent box

Highlight Length, click into Independent(s) box

Under Block 1 of 1, click Next

Highlight Gender recoded, click into Independent(s) box in Block 2 of 2

Method = Enter (default)

Click OK

Regression

Model Summary

Model	*R*	*R* square	Adjusted *R* square	Std. error of the estimate
1	0.713[a]	0.509	0.508	0.42229
2	0.741[b]	0.549	0.548	0.40474

[a] Predictors: (constant), length (cm).
[b] Predictors: (constant), length (cm), gender re-coded.

ANOVA[c]

Model		Sum of squares	*df*	Mean square	*F*	Sig.
1	Regression	101.119	1	101.119	567.043	0.000[a]
	Residual	97.723	548	0.178		
	Total	198.842	549			
2	Regression	109.235	2	54.617	333.407	0.000[b]
	Residual	89.607	547	0.164		
	Total	198.842	549			

[a] Predictors: (constant), length (cm).
[b] Predictors: (constant), length (cm), gender re-coded.
[c] Dependent variable: weight (kg).

Coefficients[a]

		Unstandardised coefficients		Standardised coefficients		
Model		*B*	Std. error	Beta	*t*	Sig.
1	(Constant)	−5.412	.0411		−13.167	0.000
	Length (cm)	0.178	0.007	0.713	23.813	0.000
2	(Constant)	−4.563	0.412		−11.074	0.000
	Length (cm)	0.165	0.007	0.660	22.259	0.000
	Gender re-coded	−0.251	0.036	−0.209	−7.039	0.000

[a] Dependent variable: weight (kg).

Excluded Variables[b]

						Collinearity statistics
Model		Beta In	*t*	Sig.	Partial correlation	Tolerance
1	Gender re-coded	−0.209[a]	−7.039	0.000	−0.288	0.936

[a] Predictors in the model: (constant), length (cm).
[b] Dependent variable: weight (kg).

The Model Summary table indicates the strength of the predictive or explanatory variables in the regression model. The first model contains length and the second model contains length and gender. Because there are a different number of variables in the two models, the adjusted R square value is used when making direct comparisons between the models. The adjusted R square value can be used to assess whether the fit of the model improves with inclusion of the additional variable, that is whether the amount of explained variation increases. By comparing the adjusted R square of Model 1 generated in Block 1 with the adjusted R square of Model 2 generated in Block 2, it is clear that adding gender improves the model fit because the adjusted R square increases from 0.508 to 0.548. This indicates that 54.8% of the variation is now explained. If it is important to know whether the R square increases by a significant amount, a P value for the change can be obtained by using the following commands *Regression → Linear → Statistics → R squared change*.

In the ANOVA table, the regression mean square decreases from 101.119 in Model 1 to 54.617 in Model 2 when gender is added because more of the unexplained variation is now explained. With high F values, both models are clearly significant as expected.

In the Coefficients table, the standard error around the beta coefficient for length (B) remains at 0.007 in both models indicating that the model is stable. An increase of more than 10% in a standard error indicates collinearity between the variables in the model and the variable being added.

With two explanatory variables in the model, the regression line will be of the form of $y = a + b_1x_1 + b_2x_2$, where $x_1$is length and x_2 is gender. Substituting the variables and the unstandardised coefficients from the Coefficients table, the equation for model is as follows:

$$\text{Weight} = -4.563 + (0.165 \times \text{Length}) - (0.251 \times \text{Gender})$$

Because males are coded zero, the final term in the equation is removed for males. The term for gender indicates that, after adjusting for length, females are 0.251 kg lighter than males. In effect this means that the y intercept is –4.563 for males and –4.814 (i.e. –4.563 – 0.251) for females. Thus the lines for males and females are parallel but females have a lower y-axis intercept.

The unstandardised coefficients cannot be directly compared to assess their relative importance because they are in the original units of the measurements. However, the standardised coefficients indicate the relative importance of each variable in comparable standardised units (z scores). The Coefficients table shows that length with a standardised coefficient of 0.660 is a more significant predictor of weight than gender with a standardised coefficient of –0.209. As with an R value, the negative sign is an indication of the direction of effect only. The standardised coefficients give useful additional information because they show that although both predictors have the same P values, they are not of equal importance in predicting weight.

The Excluded Variables table shows the model with gender omitted. The beta ln is the standardised coefficient that would result if gender is included in the model and is identical to the standardised coefficient in the Coefficients table above. The partial correlation is the unique contribution of gender to predicting weight after the effect of length is removed and is an estimate of the relative importance of this predictive variable in isolation from length. The collinearity statistic tolerance is close to 1 indicating that the predictor variables are not closely related to one another and that the regression assumption of independence between predictive variables is not violated.

Plotting a regression line with categorical explanatory variables

To plot a regression equation, it is important to ascertain the range of the explanatory variable values because the line should never extend outside the absolute range of the data. To obtain the minimum and maximum values of length for males and females the commands *Analyze → Compare Means → Means* can be used with length as the dependent variable and gender2 as the independent variable, and *Options* clicked to request minimum and maximum values. This provides the information that the length of male babies ranges from 50 to 62 cm and that the length of female babies ranges from 48 to 60.5 cm.

Table 6.2 shows how an Excel spreadsheet can be used to compute the coordinates for the beginning and end of the regression line for each gender. The regression coefficients from the equation are entered in the first three columns, and the minimum and maximum values for length and indicators of gender are entered in the next two columns. Weight is then calculated using the equation of the regression line and the calculation function in Excel.

Table 6.2 Excel spreadsheet to calculate regression line coordinates

Column 1	Column 2	Column 3	Column 4	Column 5	Column 6
a	b1	b2	length	gender2	predicted weight
−4.563	0.165	−0.251	50	0	3.687
−4.563	0.165	−0.251	62	0	5.667
−4.563	0.165	−0.251	48	1	3.106
−4.563	0.165	−0.251	60.5	1	5.169

The line coordinates from columns 4 and 6 can be copied and pasted into SigmaPlot to draw the graph using the commands shown in Box 6.9. The SigmaPlot spreadsheet should have the lower and upper coordinates for males in columns 1 and 2 and the lower and upper coordinates for females in columns 3 and 4 as follows:

Column 1	Column 2	Column 3	Column 4
50.0	3.69	48.0	3.11
62.0	5.67	60.5	5.17

Box 6.9 SigmaPlot commands to plot regression lines

SigmaPlot Commands

SigmaPlot – [Data 1]*

Graph → Create Graph

Create Graph – Type

Highlight 'Line Plot', click Next

Create Graph – Style

Highlight 'Simple Straight Line', click Next

Create Graph – Data Format

Data format = Highlight 'XY Pair', click Next

Create Graph – Select Data

Highlight Column 1, click into Data for X

Highlight Column 2, click into Data for Y

Click Finish

The second line for females can be added using *Graph → Add Plot* and using the same command sequence shown in Box 6.9, except that the *Data for X* is column 3 and the *Data for Y* is column 4. The resulting graph can then be customised using the many options in *Graph → Graph Properties*. The completed graph, as shown in Figure 6.4, is a useful tool for presenting summary results

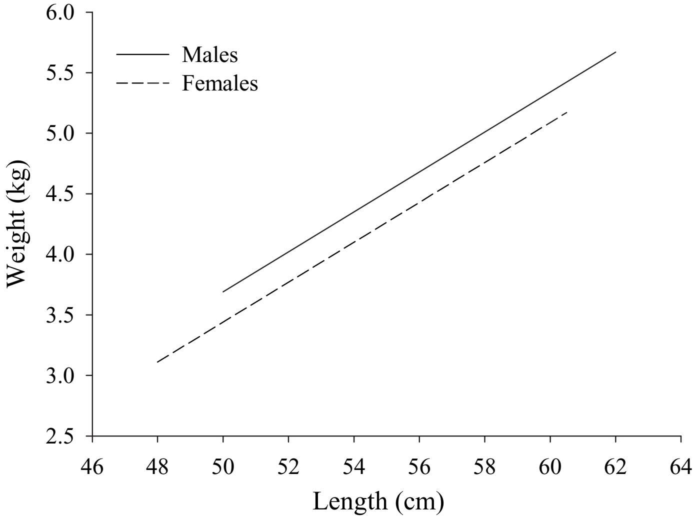

Figure 6.4 Equations for predicting weight at 1 month of age in term babies.

in a way that shows the relationship between weight and length and the size of the difference between the genders.

Regression models with two explanatory categorical variables

Having established the relation between weight, length and gender, the re-coded binary variable parity2 can be added to the model. Using the commands shown in Box 6.8, length and gender re-coded can be added as independent variables into Block 1 of 1 and parity re-coded (binary) as an independent variable into Block 2 of 2 to obtain the following output.

Regression

Model Summary

Model	*R*	*R* square	Adjusted *R* square	Std. error of the estimate
1	0.741[a]	0.549	0.548	0.40474
2	0.747[b]	0.559	0.556	0.40088

[a] Predictors: (constant), gender re-coded, length (cm).

[b] Predictors: (constant), gender re-coded, length (cm), parity re-coded.

Coefficients[a]

		Unstandardised coefficients		Standardised coefficients		
Model		B	Std. error	Beta	*t*	Sig.
1	(Constant)	−4.563	0.412		−11.074	0.000
	Length (cm)	0.165	0.007	0.660	22.259	0.000
	Gender re-coded	−0.251	0.036	−0.209	−7.039	0.000
2	(Constant)	−4.572	0.408		−11.203	0.000
	Length (cm)	0.164	0.007	0.655	22.262	0.000
	Gender re-coded	−0.255	0.035	−0.212	−7.200	0.000
	Parity re-coded (binary)	0.124	0.036	0.097	3.405	0.001

[a] Dependent variable: weight (kg).

Excluded Variables[b]

						Collinearity statistics
Model		Beta In	*t*	Sig.	Partial correlation	Tolerance
1	Parity re-coded (binary)	0.097[a]	3.405	0.001	0.144	0.997

[a] Predictors in the model: (constant), gender re-coded, length (cm).

[b] Dependent variable: weight (kg).

The Model Summary table shows that adding parity to the model improves the adjusted *R* square value only slightly from 0.548 in Model 1 to 0.556 in Model 2, that is 55.6% of the variation is now explained.

In the ANOVA table, the mean square decreases from 54.617 in Model 1 to 37.033 in Model 2 because more of the unexplained variation is now explained.

In the Coefficients table, the standard error for length remains at 0.007 in both models and the standard error for gender reduces slightly from 0.036 in Model 1 to 0.035 in Model 2 indicating that the model is stable. The unstandardised coefficients indicate that the equation for the regression model is now as follows:

$$\text{Weight} = -4.572 + (0.164 \times \text{Length}) - (0.255 \times \text{Gender}) + (0.124 \times \text{Parity})$$

When parity status is singleton, i.e. parity equals zero, the final term of the regression equation will return a zero value and will therefore be removed for singleton babies. Therefore, the model indicates that, after adjusting for length and gender, babies who have siblings are on average 0.124 kg heavier than singleton babies.

The standardised coefficients in the Coefficients table show that length and gender are more significant predictors than parity in that their standardised coefficients are larger. These coefficients give a useful estimate of the size of effect of each variable when, as in this case, the *P* values are similar.

The Excluded Variables table shows that tolerance remains high at 0.997 indicating that there is no collinearity between variables.

Plotting regression lines with two explanatory categorical variables

Figure 6.4 shows regression lines plotted for a single binary explanatory variable. To include the second binary explanatory variable of sibling status in the graph, two line coordinates are computed for each of the four groups, that is males with no siblings; males with one or more siblings; females with no siblings and females with one or more siblings. To obtain the minimum and maximum values for each of these groups, the data can be split by gender using the *Split File* command shown in Box 4.8 in Chapter 4 and then the commands *Analyze→Compare Means→Means* can be used with length as the dependent variable and parity2 as the independent variable and *Options* clicked to request minimum and maximum values.

Again, Excel can be used to calculate the regression coordinates using the regression equation and with an indicator for parity included in an additional column. The Excel spreadsheet from Table 6.3 and the commands from Box 6.9 can be used to plot the figure in SigmaPlot with additional lines included under *Graph→Add Plot*.

Table 6.3 Excel spreadsheet for calculating coordinates for regression lines with two binary explanatory variables

Column 1 a	Column 2 b1	Column 3 b2	Column 4 b3	Column 5 length	Column 6 gender2	Column 7 parity2	Column 8 predicted weight
−4.572	0.164	−0.255	0.124	50	0	0	3.63
−4.572	0.164	−0.255	0.124	62	0	0	5.60
−4.572	0.164	−0.255	0.124	49	1	0	3.21
−4.572	0.164	−0.255	0.124	58.5	1	0	4.77
−4.572	0.164	−0.255	0.124	50	0	1	3.75
−4.572	0.164	−0.255	0.124	62	0	1	5.72
−4.572	0.164	−0.255	0.124	48	1	1	3.17
−4.572	0.164	−0.255	0.124	60.5	1	1	5.22

The coordinates from columns 5 and 8 can be copied and pasted into SigmaPlot and then split and rearranged to form the following spreadsheet of line coordinates.

Line 1 – X	Line 1 – Y	Line 2 – X	Line 2 – Y	Line 3 – X	Line 3 – Y	Line 4 – X	Line 4 – Y
50.0	3.63	49.0	3.21	50.0	3.75	48.0	3.17
62.0	5.60	58.5	4.77	62.0	5.72	60.5	5.22

The SigmaPlot commands shown in Box 6.9 but with 'multiple straight lines' selected under Graph Styles can be used to draw the four regression lines as shown in Figure 6.5. Plotting the lines is a useful method to indicate the size of the differences in weight between the four groups.

Including multi-level categorical variables

The previous model includes categorical variables with only two levels, that is binary explanatory variables. A categorical explanatory variable with three or more levels can also be included in a regression model but first needs to be transformed into a series of binary variables. Simply adding a variable with three or more levels would produce a regression coefficient that indicates the effect for each level of the variable. If the effects for each level are unequal, the regression assumption that there is an equal (linear) effect across each level of the variable will be violated. Thus, multi-level categorical variables can only be used when there is a linearity of effect over the categories. This assumption of linearity is not required for ANOVA.

When there are different effects across three or more levels of a variable, the problem of non-linearity can be resolved by creating dummy variables, which are also called indicator variables. It is not possible to include a dummy variable for each level of the variable because the dummy variables would

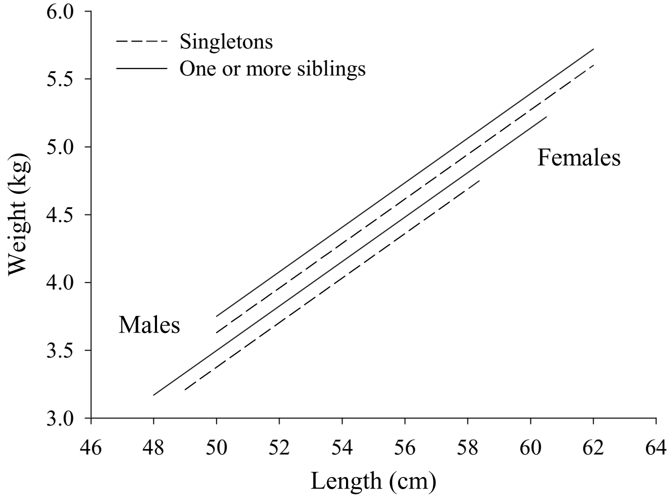

Figure 6.5 Regression lines by gender and parity status for predicting weight at 1 month of age in term babies.

lack independence and create collinearity. Therefore for *k* levels of a variable, there will be *k* – 1 dummy variables, for example for a variable with three levels two dummy variables will be created. It is helpful in interpreting the results if each dummy variable has a binary coding of 0 or 1.

The variable parity1 with three levels from Chapter 5, that is parity coded as babies with 0, 1 or 2 or more siblings, can be re-coded into dummy variables using *Transform → Recode → Into Different Variables.*

parityd1: *Old Value = 1 → New Value = copy old value (1 sibling);*
Old Value: All other values → New Value = 0
parityd2: *Old Value = 2 → New Value = 1 (2 or more siblings)*
Old Value: All other values → New Value = 0

Clearly a dummy variable for singletons is not required because if the values of parityd1 and parityd2 are both coded 0, the case is singleton. Dummy variables are invaluable for testing the effects of ordered groups that are likely to be different, for example lung function in groups of non-smokers, ex-smokers and current smokers. It is essential that dummy variables are used when groups are non-ordered, for example when marital status is categorised as single, married or divorced.

Using the SPSS commands shown in Box 6.8, length and gender2 can be added into the model as independent variables into Block 1 of 1 and the dummy variables parityd1 and parityd2 added in Block 2 of 2. Related dummy variables must always be included in a model together because they cannot be treated independently. If one dummy variable is significant in the model and a related dummy variable is not, they must both be left in the model together.

Regression

Model Summary

Model	*R*	*R* square	Adjusted *R* square	Std. error of the estimate
1	0.741[a]	0.549	0.548	0.40474
2	0.748[b]	0.559	0.556	0.40109

[a] Predictors: (constant), gender recoded, length (cm).
[b] Predictors: (constant), gender recoded, length (cm) dummy variable − parity = 1, dummy variable − parity >=2.

Coefficients[a]

Model		Unstandardised coefficients		Standardised coefficients		
		B	Std. error	Beta	*t*	Sig.
1	(Constant)	−4.563	0.412		−11.074	0.000
	Length (cm)	0.165	0.007	0.660	22.259	0.000
	Gender recoded	−0.251	0.036	−0.209	−7.039	0.000
2	(Constant)	−4.557	0.409		−11.144	0.000
	Length (cm)	0.164	0.007	0.654	22.182	0.000
	Gender recoded	−0.255	0.035	−0.212	−7.216	0.000
	Dummy variable − parity = 1	0.111	0.042	0.088	2.678	0.008
	Dummy variable − parity >= 2	0.138	0.043	0.108	3.249	0.001

[a] Dependent variable: weight (kg).

Excluded Variables[b]

Model		Beta In	*t*	Sig.	Partial correlation	Collinearity statistics
						Tolerance
1	Dummy variable − parity = 1	0.034[a]	1.188	0.236	0.051	0.999
	Dummy variable − parity >= 2	0.063[a]	2.183	0.029	0.093	0.994

[a] Predictors in the model: (constant), gender re-coded, length (cm).
[b] Dependent variable: weight (kg).

In the Model Summary table, the adjusted *R* square value shows that the addition of the dummy variables for parity improves the fit of the model only slightly from 0.548 to 0.556, that is by 0.8%. In the Coefficients table, the *P* values for the unstandardised coefficients show that both dummy variables are significant predictors of weight with *P* values of 0.008 and 0.001 respectively. However, the low standardised coefficients and the small partial correlations in the Excluded Variables table show that the dummy variables contribute little to the model compared to length and gender.

The regression equation shown in the Coefficients table is now as follows:

$$\begin{aligned}\text{Weight} = {} & -4.557 + (0.164 \times \text{Length}) - (0.255 \times \text{Gender}) \\ & + (0.111 \times \text{Parityd1}) + (0.138 \times \text{Parityd2})\end{aligned}$$

Because of the binary coding used, the final two terms in the model are rendered zero for singletons because both dummy variables are coded zero. The coefficients for the final two terms indicate that after adjusting for length and gender, babies with one sibling are on average 0.111 kg heavier than singletons, and babies with two or more siblings are on average 0.138 kg heavier than singletons.

Multiple linear regression with two continuous variables and two categorical variables

Any combination of continuous and categorical explanatory variables can be included in a multiple linear regression model. The previous regression model with one continuous and two categorical variables, that is length, gender and parity, can be further extended with the addition of second continuous explanatory variable, that is head circumference.

Research question

Using the file **weights.sav**, the research question can be extended to examine whether head circumference contributes to the prediction of weight in 1 month old babies after adjusting for length, gender and parity. The final predictive equation could be used to generate normal values for term babies, to calculate *z* scores for babies' weights, or to calculate per cent predicted weights.

The regression model obtained previously can be built on to test the influence of the variable, head circumference. The model in which parity2 was included as a binary variable is used because including parity with three levels coded as dummy variables did not substantially improve the fit of the model. Using the SPSS commands shown in Box 6.8, length, gender2 and parity2 can be added in Block 1 of 1and head circumference in Block 2 of 2 to generate the following output.

Regression

Model Summary

Model	*R*	*R* square	Adjusted *R* square	Std. error of the estimate
1	0.747[a]	0.559	0.556	0.40088
2	0.772[b]	0.596	0.593	0.38406

[a] Predictors: (constant), parity re-coded, gender re-coded, length (cm).

[b] Predictors: (constant), parity re-coded, gender re-coded, length (cm), head circumference (cm).

Coefficients[a]

		Unstandardised coefficients		Standardised coefficients		
Model		***B***	**Std. error**	**Beta**	***t***	**Sig.**
1	(Constant)	−4.572	0.408		−11.203	0.000
	Length (cm)	0.164	0.007	0.655	22.262	0.000
	Gender re-coded	−0.255	0.035	−0.212	−7.200	0.000
	Parity re-coded (binary)	0.124	0.036	0.097	3.405	0.001
2	(Constant)	−6.890	0.511		−13.496	0.000
	Length (cm)	0.130	0.009	0.520	15.243	0.000
	Gender re-coded	−0.196	0.035	−0.163	−5.624	0.000
	Parity re-coded (binary)	0.093	0.035	0.073	2.638	0.009
	Head circumference (cm)	0.110	0.016	0.249	7.061	0.000

[a] Dependent variable: weight (kg).

Excluded Variables[b]

						Collinearity statistics
Model		**Beta In**	***t***	**Sig.**	**Partial correlation**	**Tolerance**
1	Head circumference (cm)	0.249[a]	7.061	0.000	0.290	0.598

[a] Predictors in the model: (constant), parity re-coded (binary), gender re-coded, length (cm).
[b] Dependent variable: weight (kg).

The Model Summary table shows that the adjusted *R* square increases slightly from 55.6% to 59.3% with the addition of head circumference. In the Coefficients table, all predictors are significant and the standardised coefficients show that length contributes to the model to a greater degree than head circumference, but that head circumference makes a larger contribution than gender or parity. However, the tolerance statistic in the Excluded Variables has fallen to 0.598 indicating some collinearity in the model. This is expected because the initial Pearson's correlations showed a significant association between length and head circumference with an *r* value of 0.598. As a result of the collinearity, the standard error for length has inflated from 0.007 in Model 1 to 0.009 in Model 2, a 29% increase. The benefit of explaining an extra 3.7% of the variation in length has to be balanced with this loss of precision.

Deciding which variables to include in a model can be difficult. Head circumference is expected to vary with length as a result of common factors that influence body size and growth. In this situation, head circumference should be classified as an alternative outcome rather than an independent explanatory variable because it is on the same developmental pathway as length.

Each model building situation will be different but it is important that the relationships between the variables and the purpose of building the model are always carefully considered.

Interactions

An interaction occurs when there is a multiplicative rather than additive relationship between two variables. An additive effect of a binary variable was shown in Figure 6.4 where the lines for each gender had the same slopes so that they were parallel. If an interactive effect is present, the two lines would have different slopes and would cross over or intersect at some point[9].

Again, coding of binary variables as 0 and 1 is helpful for interpreting interactions. In the following equation, which shows an interaction between length and gender, the third and fourth terms in the model will be zero when gender is coded 0. When gender is coded as 1, the third term will add a fixed amount to the prediction of the outcome variable and the fourth interactive term will add an amount that increases as length increases thereby causing the regression lines for each gender to increasingly diverge.

$$\text{Weight} = a + (b_1 \times \text{Length}) + (b_2 \times \text{Gender}) + (b_3 \times \text{Length} \times \text{Gender})$$

It is preferable to explore evidence that an interaction is present rather than testing for all possible interactions in the model. Testing for all interactions will almost certainly throw up some spurious but significant P values[10]. Interactions naturally introduce collinearity into the model because the interaction term correlates with both of its derivatives. This will result in an unstable model, especially when the sample size is small.

Interactions between variables can be identified by plotting the dependent variable against the explanatory variable for each group within a factor. The regression plots can then be inspected to assess whether there is a different linear relationship across the groups. To obtain the plots shown in Figure 6.6, the SPSS commands shown in Box 6.7 can be used with gender2 highlighted and dragged into the *Panel Variables* box and accepted for conversion to a categorical variable. Prediction lines are not requested.

The regression equations shown in Figure 6.6 indicate that the y intercept is different for males and females as expected from the former regression equations. When they values of the data points are a long way from zero, as in these plots, the intercept has no meaningful interpretation although they can indicate that the slopes are different. However, the slope of the line through the points is similar at 0.19 for males and 0.13 for females. This similarity of slopes suggests that there is no important interaction between length and gender in predicting weight. The graphs can be repeated to investigate a possible interaction between head circumference and gender.

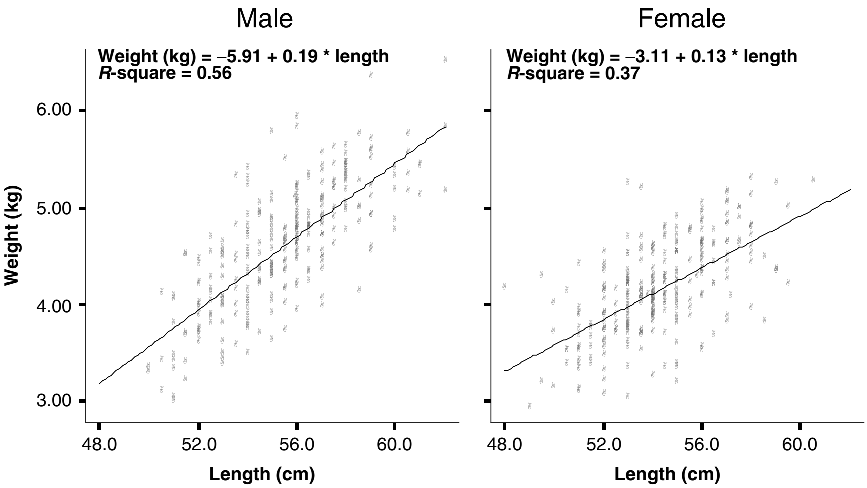

Figure 6.6 Scatter plots of weight on length for male and female babies with regression line.

The plots in Figure 6.7 show that the intercept is different between the genders at −6.75 for males and −3.22 for females. Moreover, the slope of 0.30 for males is 50% higher than the slope of 0.20 for females as shown by the different slopes of the regression lines through the plots. If plotted on the same figure, the two regression lines would intersect at some point indicating an interaction between head circumference and gender. The interaction term can be computed for inclusion in the model as shown in Box 6.10.

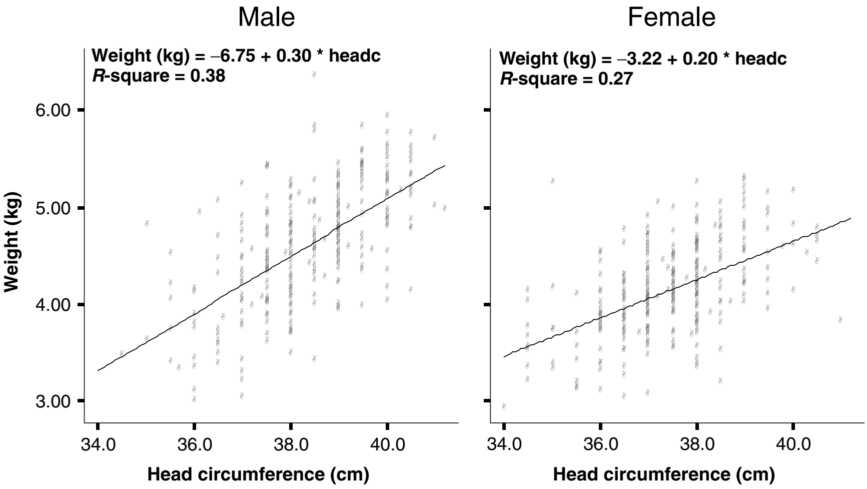

Figure 6.7 Scatter plots of weight on head circumference for male and female babies with regression line.

Box 6.10 SPSS command to compute an interaction term

SPSS Commands

weights – SPSS Data Editor
    Transform → Compute
Compute Variable
    Target Variable = headxgen
    *Numeric Expression = Head circumference * Gender recoded*
    Click OK

In practice, head circumference would be omitted from the model because of its collinearity with length but it is included in this model solely for demonstrating the effect of an interaction term. The model is obtained using the commands shown in Box 6.8 and by adding length, gender2, parity2 and head circumference into Block 1 of 1 and the interaction term headxgen into Block 2 of 2.

Regression

Model Summary

Model	*R*	*R* square	Adjusted *R* square	Std. error of the estimate
1	0.772[a]	0.596	0.593	0.38406
2	0.775[b]	0.601	0.597	0.38211

[a] Predictors: (constant), head circumference (cm), parity re-coded (binary), gender re-coded, length (cm).
[b] Predictors: (constant), head circumference (cm), parity re-coded (binary), gender re-coded, length (cm), head by gender interaction.

Coefficients[a]

		Unstandardised coefficients		Standardised coefficients		
Model		*B*	Std. error	Beta	*t*	Sig.
1	(Constant)	−6.890	0.511		−13.496	0.000
	Length (cm)	0.130	0.009	0.520	15.243	0.000
	Gender re-coded	−0.196	0.035	−0.163	−5.624	0.000
	Parity re-coded (binary)	0.093	0.035	0.073	2.638	0.009
	Head circumference (cm)	0.110	0.016	0.249	7.061	0.000
2	(Constant)	−8.086	0.689		−11.731	0.000
	Length (cm)	0.128	0.009	0.512	15.034	0.000
	Gender re-coded	2.282	0.966	1.898	2.362	0.019
	Parity re-coded (binary)	0.093	0.035	0.073	2.651	0.008
	Head circumference (cm)	0.144	0.020	0.326	7.063	0.000
	Head by gender interaction	−0.065	0.025	−2.040	−2.567	0.011

[a] Dependent variable: weight (kg).

Excluded Variables[b]

						Collinearity statistics
Model		**Beta In**	***t***	**Sig.**	**Partial correlation**	**Tolerance**
1	Head by gender interaction	−2.040[a]	−2.567	0.011	−0.109	0.001

[a] Predictors in the model: (constant), head circumference (cm), parity re-coded (binary), gender re-coded, length (cm).
[b] Dependent variable: weight (kg).

The Model Summary table shows that the interaction term only slightly improves the fit of the model by increasing the adjusted *R* square from 0.593 to 0.597. In the Coefficients table, the interaction term in Model 2 is significant with a *P* value of 0.011 and therefore must be included because it helps to describe the true relationship between weight, head circumference and gender. If an interaction term is included then both derivative variables, that is head circumference and gender, must be retained in the model regardless of their statistical significance. Once an interaction is present, the coefficients for the derivative variables have no interpretation except that they form an integral part of the mathematical equation.

The Coefficients table shows that inclusion of the interaction term inflates the standard error for head circumference from 0.016 in Model 1 to 0.02 in Model 2 and significantly inflates the standard error for gender from 0.035 to 0.966. These standard errors have inflated as a result of the collinearity with the interaction term and, as a result, the tolerance value in the Excluded Variables table is very low and unacceptable at 0.001, also a sign of collinearity. This example highlights the trade-off between building a stable predictive model and deriving an equation that describes an interaction between variables. Collinearity caused by interactions can be removed by a technique called centreing[7], which is described later in this chapter but is rarely used in the literature.

Model of best fit

The final model with all variables and the interaction term included could be considered to be over-fitted. By including variables that explain little additional variation and by including the interaction term, the model not only becomes complex but the precision around the estimates is sacrificed and the regression assumptions of independence are violated. Head circumference should be omitted because of its relation with length and because it explains only a small additional amount of variation in weight. Thus, the interaction term is also omitted. The final model with only length, gender and parity is parsimonious. Once the final model is reached, the remaining regression assumptions should be confirmed.

Residuals

The residuals are the distances between each data point and the value predicted by the regression equation, that is the variation about the regression line shown in Figure 6.2. The residual distances are converted to standardised residuals that are in units of standard deviations from the regression. Standardised residuals are assumed to be normal or approximately normally distributed with a mean of zero and a standard deviation of 1.

Given the characteristics of a normal distribution, it is expected that 5% of standardised residuals will be outside the area that lies between −1.96 and +1.96 standard deviations from the mean (see Figure 2.2). In addition, 1% of standardised residuals are expected to be outside the area that lies between −3 and +3 standard deviations from the mean.

As the sample size increases, there will be an increasing number of potential outliers. In this sample size of 550 babies, it is expected that 5 children will have a standardised residual that will be outside the area that lies between −3 and +3 standard deviations from the mean.

An assumption of regression is that the residuals are normally distributed. The residual for each case can be saved to a data column using the *Save* option and the plots of the residuals can be obtained while running the model as shown in Box 6.11. The normality of the residuals can then be inspected using *Analyze* →*Descriptive Statistics* →*Explore* as discussed in Chapter 2.

Box 6.11 SPSS commands to test the regression assumptions

SPSS Commands

weights – SPSS Data Editor

Analyze → Regression → Linear

Linear Regression

Highlight Weight, click into the Dependent box

Highlight Length, Gender recoded, Parity recoded (binary), click into the Independent(s) box

Click on Statistics

Linear Regression: Statistics

Under Regression Coefficients, tick Estimates (default)

Tick Model fit (default) and Collinearity diagnostics

Under Residuals, tick Casewise diagnostics – Outliers outside 3 standard deviations (default), click Continue

Linear Regression

Click Plots

Linear Regression: Plots

*Under Scatter 1 of 1, highlight *ZPRED and click into X; highlight *ZRESID and click into Y*

Under Standardized Residual Plots, tick Histogram and Normal probability plot

Click Continue

Linear Regression
Click on Save
Linear Regression: Save
Under Predicted Values, tick Standardized
Under Residuals, tick Standardized
Under Distances, tick Mahalanobis, Cook's and Leverage values
Click Continue
Linear Regression
Click OK

Regression

Coefficients[a]

		Unstandardised coefficients		Standardised coefficients			Collinearity statistics	
Model		***B***	**Std. error**	**Beta**	***t***	**Sig.**	**Tolerance**	**VIF**
1	(Constant)	−4.572	0.408		−11.203	0.000		
	Length (cm)	0.164	0.007	0.655	22.262	0.000	0.933	1.071
	Gender re-coded	−0.255	0.035	−0.212	−7.200	0.000	0.935	1.069
	Parity re-coded	0.124	0.036	0.097	3.405	0.001	0.997	1.003

[a] Dependent variable: weight (kg).

Casewise diagnostics[a]

Case number	Std. residual	Weight (kg)	Predicted value	Residual
243	3.122	5.23	3.9783	1.2517

[a] Dependent variable: weight (kg).

Residual Statistics[a]

	Minimum	Maximum	Mean	Std. deviation	*N*
Predicted value	3.1594	5.7069	4.3664	0.44985	550
Std. predicted value	−2.683	2.980	0.000	1.000	550
Standard error of predicted value	0.02687	0.06017	0.03365	0.00604	550
Adjusted predicted value	3.1413	5.7047	4.3665	0.44988	550
Residual	−1.0791	1.2517	0.0000	0.39978	550
Std. residual	−2.692	3.122	0.000	0.997	550
Stud. residual	−2.706	3.130	0.000	1.001	550
Deleted residual	−1.0904	1.2581	−0.0001	0.40276	550
Stud. deleted residual	−2.722	3.156	0.000	1.003	550
Mahal. distance	1.469	11.372	2.995	1.529	550
Cook's distance	0.000	0.028	0.002	0.003	550
Centred leverage value	0.003	0.021	0.005	0.003	550

[a] Dependent variable: weight (kg).

The Coefficients table shows the variables in the model and the high tolerance values confirm their lack of collinearity. The Casewise Diagnostics table shows the cases that are more than three standard deviations from the regression line. There is only one case that has a standardised residual that is more than three standard deviations from the regression, that is case number 243 which is a baby with a weight of 5.23 kg compared with a predicted value of 3.9783 kg and with a standardised residual of 3.122.

The Residuals Statistics table shows the minimum and maximum predicted values. The predicted values range from 3.159 to 5.707 kg and the unstandardised residuals range from 1.079 kg below the regression line to 1.252 kg above the regression line. This is the minimum and maximum distances of babies from the equation, which is the variation about the regression.

The standardised predicted values and standardised residuals shown in the Residuals Statistics table are expressed in units of their standard deviation and have a mean of zero and a standard deviation of approximately or equal to 1, as expected when they are normally distributed.

The histogram and normal P–P plot shown in Figure 6.8 indicate that the distribution of the residuals deviates only slightly from a classically bell shaped distribution.

The variance around the residuals can also be used to test whether the model violates the assumption of homoscedasticity, that is equal variance over the length of the regression model. Residual plots are a good method for examining the spread of variance. The scatter plot in Figure 6.8 shows that there is an equal spread of residuals across the predicted values indicating that the model is homoscedastic.

Outliers and remote points

Outliers are data points that are more than three standard deviations from the regression line. Outliers in regression are identified in a similar manner to outliers in ANOVA. Univariate outliers should be identified before fitting a model but multivariate outliers, if present, are identified once the model of best fit is obtained. Outliers that cause a poor fit degrade the predictive value of the regression model; however, this has to be balanced with loss of generalisability if the points are omitted.

Multivariate outliers are data values that have an extreme value on a combination of explanatory variables and exert too much leverage and/or discrepancy (see Figure 5.10 in Chapter 5). Data points with high leverage and low discrepancy have no effect on the regression line but tend to increase the R square value and reduce the standard errors. On the other hand, data points with low leverage and high discrepancy tend to influence the intercept but not the slope of the regression or the R square value and tend to inflate the standard errors. Data points with both a high leverage and a high discrepancy influence the slope, the intercept and the R square value. Thus, a model that

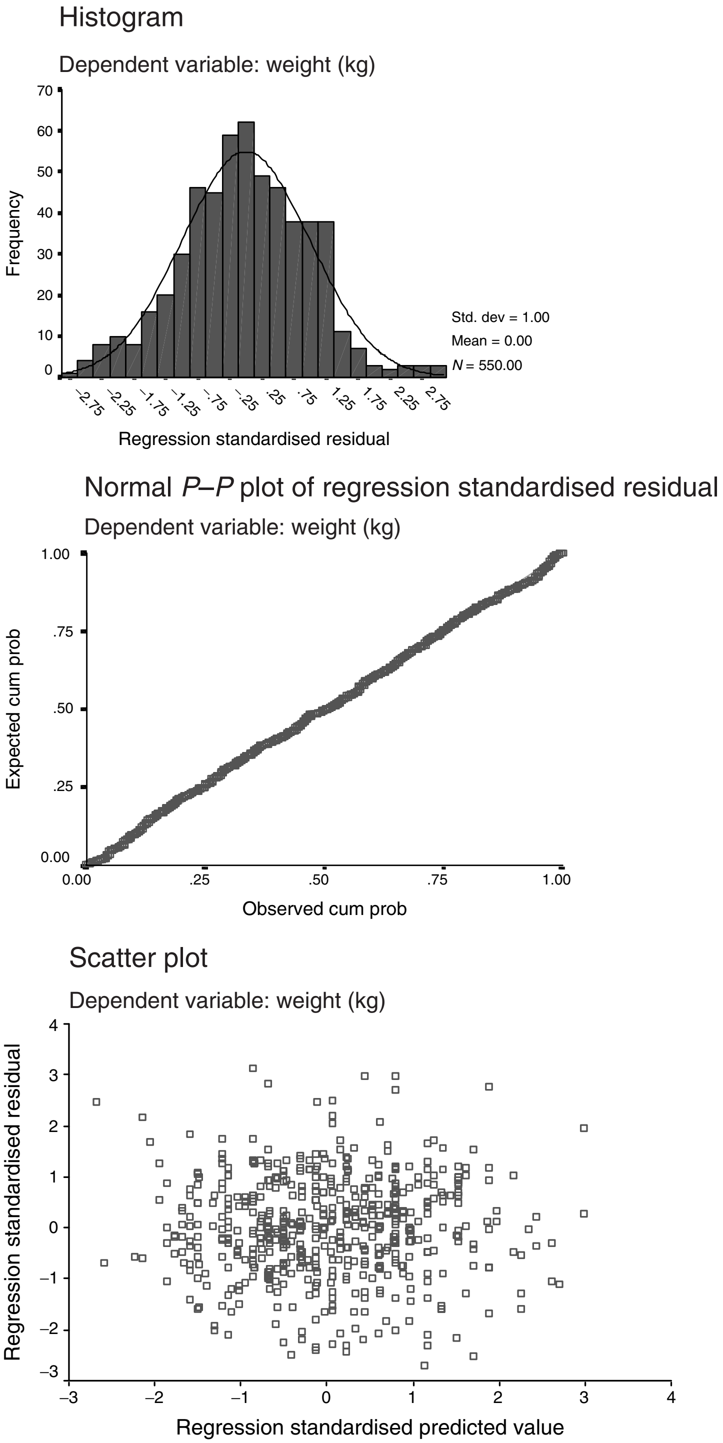

Figure 6.8 Plots of standardised residuals for regression on weight.

contains problematic data points with high leverage and/or high discrepancy values may not generalise well to the population.

Multivariate outliers can be identified using Cook's distances and leverage values as discussed in Chapter 5. The Residuals Statistics table shows that the largest Cook's distance is 0.028, which is below the critical value of 1, and the largest leverage value is 0.021, which is below the critical value of 0.05 indicating that there are no influential outliers in this model. In regression, Mahalanobis distances can also be inspected. Mahalanobis distances are evaluated using critical values of chi-square with degrees of freedom equal to the number of explanatory variables in the model. To adjust for the number of variables being tested, Mahalanobis distances are usually considered unacceptable at the $P < 0.001$ level, although the influence of any values with $P < 0.05$ should be examined.

To plot the Mahalanobis distances, which have been saved to a column at the end of the data sheet, the commands Graphs → Histogram can be used to obtain Figure 6.9. Any Mahalanobis distance that is greater than 16.266, that is a chi-square value for $P < 0.001$ with three degrees of freedom (because there are three explanatory variables in the model), would be problematic. The graph shows that no Mahalanobis distances are larger than this. This is confirmed in the Residual Statistics table, which shows that the maximum Mahalanobis distance is 11.372.

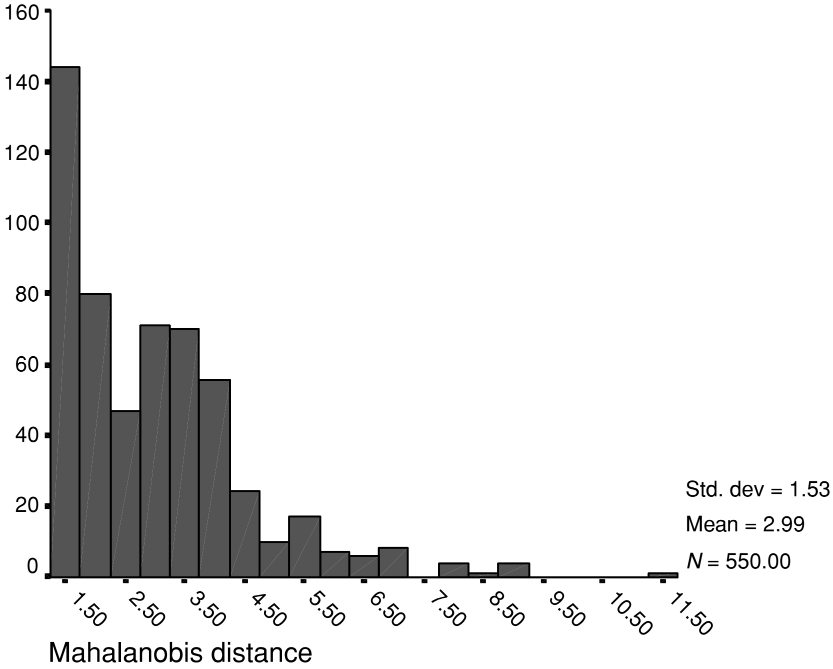

Figure 6.9 Histogram of Mahalanobis distances for weight.

If multivariate outliers are detected they can be deleted but it is not reasonable to remove troublesome data points simply to improve the fit of the model. In addition, when one extreme data point is removed another may take its place so it is important to recheck the data after deletion to ensure that there are no further multivariate outliers. Alternatively, the data can be transformed to reduce the influence of the multivariate outlier or the extreme data point can be re-coded to a less extreme value. However, a multivariate outlier depends on a combination of explanatory variables and therefore the scores would have to be adjusted for each variable. Any technique that is used to deal with multivariate outliers should be recorded in the study handbook and described in any publications.

Validating the model

If the sample size is large enough, the model can be built using one-half of the data and then validated with the other half. If this is the purpose, the sample should be split randomly. Other selections of 60% to 80% for building the model and 40% to 20% for validation can be used. A model built using one part of the data and validated using the other part of the data provides good evidence of stability and reliability. However, both models must have an adequate sample size and must conform to the assumptions for regression to minimise collinearity and maximise precision and stability.

Non-linear regression

If scatter plots suggest that there is a curved relationship between the explanatory and outcome variables, then a linear model may not be the best fit. Other non-linear models that may be more appropriate for describing the relationship can be examined using the SPSS commands shown in Box 6.12. Logarithmic, quadratic and exponential fits are the most common transformations

Box 6.12 SPSS commands for examining the equation that best fits the data

SPSS Commands
weights – SPSS Data Editor
Analyze → Regression → Curve Estimation
Curve Estimation
Highlight Weight, click into Dependent(s) box
Highlight Length, click into Independent Variable box
Under Models, tick Linear (default), Logarithmic, Quadratic and Exponential
Click OK

used in medical research when data are skewed or when a relationship is not linear.

Curve fit

```
Independent:   LENGTH

  Dependent  Mth   Rsq  d.f.        F  Sigf        b0       b1      b2

   WEIGHT    LIN  .509   548  567.04  .000  -5.4121    .1783
   WEIGHT    LOG  .508   548  566.40  .000  -34.875  9.8019
   WEIGHT    QUA  .509   547  283.03  .000  -6.6256    .2224  -.0004
   WEIGHT    EXP  .503   548  555.23  .000     .4578   .0409
```

In the Curve Fit table, b0 is the intercept which is the coefficient labelled ‘a’ in previous models. The equations of the models are as follows:

$$
\begin{aligned}
\text{Linear:}\quad & \text{Weight} = b_0 + (b_1 \times \text{Length})\\
\text{Logarithmic:}\quad & \text{Weight} = b_0 + (b_1 \times \log_e \text{Length})\\
\text{Quadratic:}\quad & \text{Weight} = b_0 + (b_1 \times \text{Length}) + (b_2 \times \text{Length}^2)\\
\text{Exponential:}\quad & \text{Weight} = b_0 + (b_1 \times e^{\text{length}})
\end{aligned}
$$

The R square values, denoted as Rsq in the Curve Fit table, show that the linear and the quadratic models have the best fit with R square values of 0.509 closely followed by the logarithmic model with an R square of 0.508. The plots in Figure 6.10 show that the curves for the four models only deviate at the extremities of the data points, which are the regions in which prediction

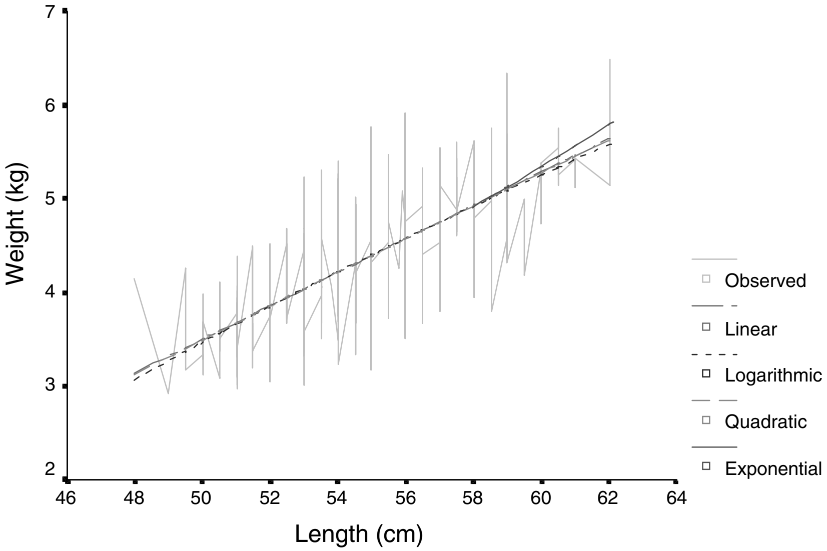

Figure 6.10 Different curve estimates of weight on length.

is less certain. Because the linear model is easier to communicate, in practice it would be the preferable model to use.

If it was important to use the quadratic model, say to compare with other quadratic models in the literature, then the square of length can be computed as lensq in the menu *Transform* → *Compute* using the formula lensq = length × length. The quadratic equation can be obtained using the commands shown in Box 6.8, with length added as independent variable into Block 1 of 1 and the square of length (lensq) into Block 2 of 2.

Model Summary

Model	***R***	***R* square**	**Adjusted *R* square**	**Std. error of the estimate**
1	0.713[a]	0.509	0.508	0.42229
2	0.713[b]	0.509	0.507	0.42266

[a] Predictors: (constant), length (cm).

[b] Predictors: (constant), length (cm), length squared.

Coefficients[a]

		Unstandardised coefficients		**Standardised coefficients**		
Model		***B***	**Std. error**	**Beta**	***t***	**Sig.**
1	(Constant)	−5.412	0.411		−13.167	0.000
	Length (cm)	0.178	0.007	0.713	23.813	0.000
2	(Constant)	−6.626	7.053		−0.939	0.348
	Length (cm)	0.222	0.256	0.890	0.868	0.386
	Length squared	0.000	0.002	−0.177	−0.172	0.863

[b] Dependent variable: weight (kg).

Excluded Variables[b]

						Collinearity statistics
Model		**Beta In**	***t***	**Sig.**	**Partial correlation**	**Tolerance**
1	Length squared	−0.177[a]	−0.172	0.863	−0.007	0.001

[a] Predictors in the model: (constant), length (cm).

[b] Dependent variable: weight (kg).

The Model Summary and Coefficients tables show that the *R* square and the regression coefficients are as indicated in the curve fit procedure. However, the standard error for length has increased from 0.007 in Model 1 to 0.256 in Model 2. In addition, length is no longer significant in Model 2 and the Excluded Variables table shows that tolerance is very low at 0.001 indicating that the explanatory variables are highly related to one other.

Collinearity can occur naturally when a quadratic term is included in a regression equation because the variable and its square are related. A scatter plot using the SPSS commands *Graphs → Scatter → Simple* to plot length squared against length demonstrates the direct relationship between the two variables as shown in Figure 6.11.

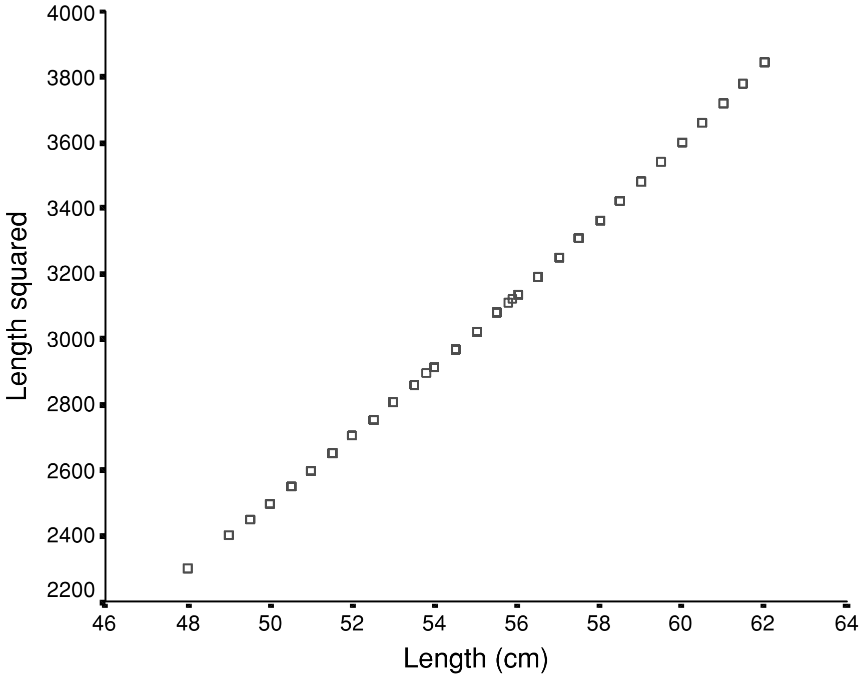

Figure 6.11 Scatter plot of length by length squared.

Centreing

To avoid collinearity in quadratic equations, a simple mathematical trick of centreing, that is subtracting a constant from the data values, can be applied[11]. The constant that minimises collinearity most effectively is the mean value of the variable. Using *Descriptive Statistics → Descriptives* in SPSS indicates that the mean of length is 54.841 cm. Using the commands *Transform → Compute* the mean value is used to compute a new variable for length centred (lencent) as length – 54.841 and then to compute another new variable which is the square of lencent (lencntsq).

A scatter plot of length centred and its square in Figure 6.12 shows that the relationship is no longer linear simply because subtracting the mean value gives half of the values a negative value but then squaring all values returns a positive value again. The relation is thus U-shaped and no longer linear.

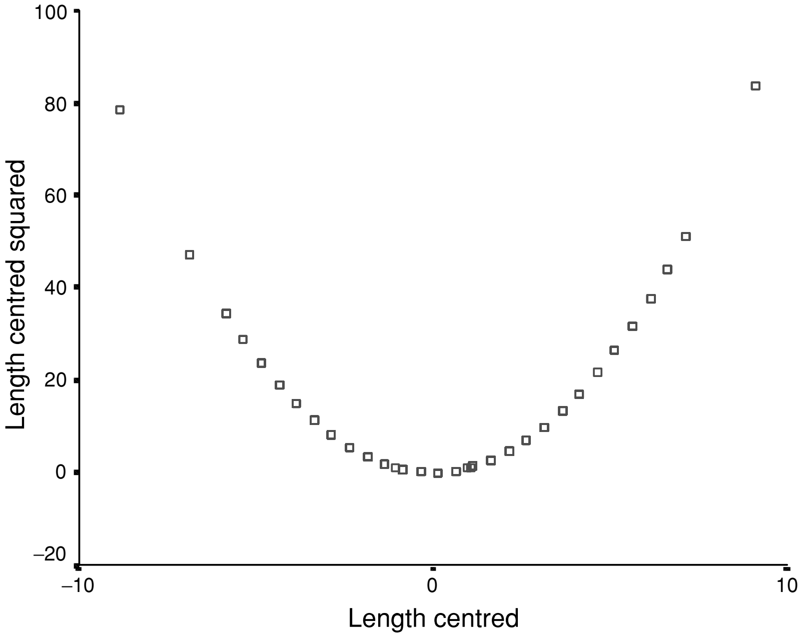

Figure 6.12 Scatter plot of length squared by length centred squared.

The regression can now be re-run using the commands shown in Box 6.8 but with length centred in Block 1 of 1 and its square in Block 2 of 2.

Model Summary

Model	*R*	*R* square	Adjusted *R* square	Std. error of the estimate
1	0.713[a]	0.509	0.508	0.42229
2	0.713[b]	0.509	0.507	0.42266

[a] Predictors: (constant), length centred.

[b] Predictors: (constant), length centred, length centred squared.

Coefficients[a]

		Unstandardised coefficients		Standardised coefficients		
Model		*B*	Std. error	Beta	*t*	Sig.
1	(Constant)	4.366	0.018		242.494	0.000
	Length centred	0.178	0.007	0.713	23.813	0.000
2	(Constant)	4.369	0.022		194.357	0.000
	Length centred	0.179	0.008	0.714	23.499	0.000
	Length centred squared	0.000	0.002	–0.005	–0.172	0.863

[a] Dependent variable: weight (kg).

Excluded Variables[b]

Model		Beta In	*t*	Sig.	Partial correlation	Collinearity statistics Tolerance
1	Length centred squared	−0.005[a]	−0.172	0.863	−0.007	0.973

[a] Predictors in the model: (constant), length centred.

[b] Dependent variable: weight (kg).

The Model Summary table shows that when length is centred, the *R* square value remains unchanged and the Coefficients table shows the standard error for length is similar at 0.007 in Model 1 and 0.008 in Model 2. In addition, the unstandardised coefficients are now significant and the tolerance value is high at 0.973. The unstandardised coefficient for the square term is close to zero with a non-significant *P* value indicating its negligible contribution to the model. The equation for this regression model is as follows:

$$\text{Weight} = 4.369 + (0.179 \times (\text{Length} - 54.841)) + (0.0001 \times (\text{Length} - 54.841)^2)$$

This centred model is a more stable quadratic model than the model given by the curve fit option and is therefore more reliable for predicting weight or for testing the effects of other factors on weight.

The technique of centreing can also be used to remove collinearity caused by interactions which are naturally related to their derivatives[7].

Notes for critical appraisal

Box 6.13 shows the questions that should be asked when critically appraising a paper that reports linear or multiple regression analyses.

Box 6.13 Questions to ask when critically appraising a regression analysis

The following questions should be asked when appraising published results from analyses in which regression has been used:

- Was the sample size large enough to justify using the model?
- Are the axes the correct way around with the outcome on the *y*-axis and the explanatory variable on the *x*-axis?
- Were any repeated measures from the same participants treated as independent observations?
- Were all of the explanatory variables measured independently from the outcome variable?
- Have the explanatory variables been measured reliably?

- Is there any collinearity between the explanatory variables that could reduce the precision of the model?
- Are there any multivariate outliers that could influence the regression estimates?
- Is evidence presented that the residuals are normally distributed?
- Are there sufficient data at the extremities of the regression or should the prediction range be shortened?

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CHAPTER 7
Categorical variables: rates and proportions

When the methods of statistical inference were being developed in the first half of the twentieth century, calculations were done using pencil, paper, tables, slide rules and with luck a very expensive adding machine[1].

MARTIN BLAND STATISTICIAN

Objectives

The objectives of this chapter are to explain how to:

- use the correct summary statistics for rates and proportions
- present categorical baseline characteristics correctly
- crosstabulate categorical variables and obtain meaningful percentages
- choose the correct chi-square value
- plot percentages and interpret 95% confidence intervals
- manage cells with small numbers
- use trend tests for ordered exposure variables
- convert continuous variables with a non-normal distribution into categorical variables
- calculate the number needed to treat
- calculate significance and estimate effect size for paired categorical data
- critically appraise the literature in which rates and proportions are reported

Categorical variables are summarised using statistics called rates and proportions. A rate is a number used to express the frequency of a characteristic of interest in the population, such as 1 case per 10 000. In some cases, the rate is applied to a time period such as per annum. Frequencies can also be described using summary statistics such as a percentage e.g. 20% or a proportion e.g. 0.2. Rates, percentages and proportions are frequently used for summarising information that is collected with tick box options on questionnaires.

Obtaining information about the distribution of the categorical variables in a study provides a good working knowledge of the characteristics of the sample. The spreadsheet **surgery.sav** contains data from a sample of 141 consecutive babies who were admitted to hospital to undergo surgery. The SPSS commands shown in Box 7.1 can be used to obtain frequencies and histograms for the categorical variables prematurity (1 = Premature; 2 = Term) and gender2 (1 = Male and 2 = Female). The frequencies for place of birth were obtained in Chapter 1.

Box 7.1 SPSS commands to obtain frequencies and histograms

SPSS Commands

surgery – SPSS Data Editor
    Analyze → Descriptive Statistics → Frequencies
Frequencies
    Highlight Prematurity and Gender recoded, click into Variable(s) box
    Click on Charts
Frequencies: Charts
    Chart Type: Tick Bar charts, Click Continue
Frequencies
    Click Ok

Frequency Table

Prematurity

		Frequency	Per cent	Valid per cent	Cumulative per cent
Valid	Premature	45	31.9	31.9	31.9
	Term	96	68.1	68.1	100.0
	Total	141	100.0	100.0	

Gender Recoded

		Frequency	Per cent	Valid per cent	Cumulative per cent
Valid	Male	82	58.2	58.2	58.2
	Female	59	41.8	41.8	100.0
	Total	141	100.0	100.0	

The valid per cent column in the first Frequency table indicates that 31.9% of babies in the sample were born prematurely and that 68.1% of babies in the sample were term births. The per cent and valid per cent columns are identical because all children in the sample have information of their birth status, that is there are no missing data. In journal articles and scientific reports when the sample size is greater than 100, percentages such as these are reported with one decimal place only. When the sample size is less than 100, no decimal places are used. If the sample size was less than 20 participants, percentages would not be reported (Chapter 1) although SPSS includes them on the output.

The valid per cent column in the second Frequency table indicates that there are more males than females in the sample (58.2% vs 41.8%).

The bar charts shown in Figure 7.1 are helpful for comparing the frequencies visually and are often useful for a poster or a talk. However, charts are not suitable for presenting sample characteristics in journal articles or other

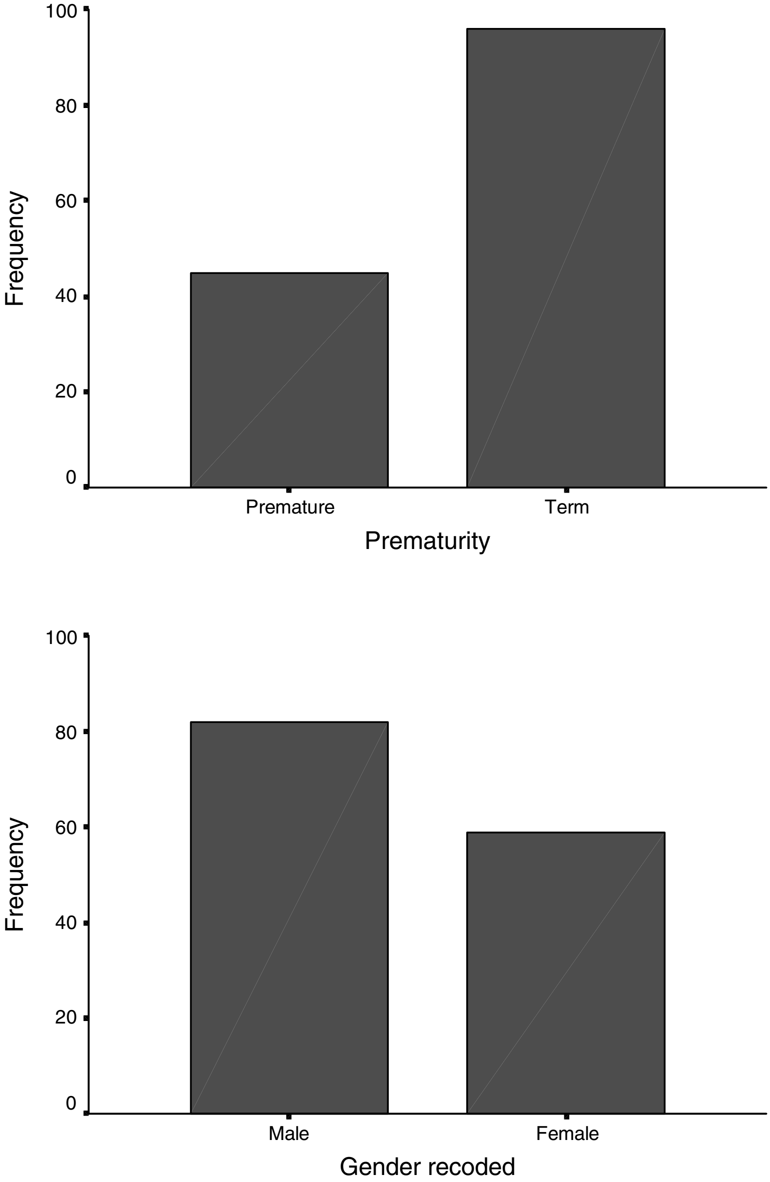

Figure 7.1 Number of babies by prematurity status and by gender.

publications because accurate frequency information cannot be read from them and they are 'space hungry' for the relatively small amount of information provided.

Baseline characteristics

The baseline characteristics of the sample could be described as shown in Table 7.1 or Table 7.2. If the percentage of male children is included, it is not necessary to report the percentage of female children because this is the complement that can be easily calculated. Similarly, it is not necessary to include percentages of both term and premature birth since one can be calculated from the other. In most cases, observed numbers are not included in addition to percentages because the numbers can be calculated from the percentages and the total number of the sample. However, some journals request that the number of cases and the sample size, e.g. 82/141, are reported in addition to percentages.

Table 7.1 Baseline characteristics

Characteristic	Per cent
Total number	*141*
Male	58.2%
Place of birth	
Local	63.8%
Regional	23.4%
Overseas	6.4%
No information	6.4%
Premature birth	31.9%

Although confidence intervals around percentage figures can be computed, these statistics are more appropriate for comparing rates in two or more different groups, as discussed later in this chapter, and not for describing the sample characteristics.

Table 7.2 Baseline characteristics

Characteristic	Sample size (*N*)	Per cent
Male	141	58.2%
Place of birth	132	
Local		68.2%
Regional		25.0%
Overseas		6.8%
Premature birth	141	31.9%

Describing categorical data

When describing frequencies, it is important to use the correct term. A common mistake is to describe prevalence as incidence, or vice versa, although these terms have different meanings and cannot be used interchangeably.

Incidence is a term used to describe the number of new cases with a condition divided by the population at risk. Prevalence is a term used to describe the total number of cases with a condition divided by the population at risk. The population at risk is the number of people during the specified time period who were susceptible to the condition. The prevalence of an illness in a specified period is the number of incident cases in that period plus the previous prevalent cases and minus any deaths or remissions.

Both incidence and prevalence are usually calculated for a defined time period, for example for a 1 or 5 year period. When the number of cases of a condition is measured at a specified point in time, the term point prevalence is used. The terms incidence and prevalence should only be used when the sample is selected randomly. When the sample has not been selected randomly from the population, the terms percentage, proportion, or frequency are more appropriate.

Chi-square tests

A chi-square test is used to assess whether the frequency of a condition is significantly different between two or more groups, for example groups who received different treatments or who have different exposures. Thus, chi-square tests would be used to assess whether there is a significant between-group difference in the frequency of participants with a certain condition. For example, chi-square could be used to test whether the absence or presence of an illness is independent of whether a child was or was not immunised.

The data for chi-square tests are summarised using crosstabulations as shown in Table 7.3. These tables are sometimes called frequency or contingency tables. Table 7.3 is called a 2 × 2 table because each variable has two levels, but tables can have larger dimensions when either the exposure or the disease has more than two levels.

Table 7.3 Crosstabulation for estimating chi-square

	Disease absent	Disease present	Total
Exposure absent	d	c	$c+d$
Exposure present	b	a	$a+b$
Total	$b+d$	$a+c$	Total

In a contingency table, one variable (usually the exposure) forms the rows and the other variable (usually the disease) forms the columns. In the above example, the exposure immunisation (no, yes) would form the rows and the illness (present, absent) would form the columns. The four internal cells of the table show the counts for each of the disease/exposure groups, for example cell '*a*' shows the number who satisfy exposure present (immunised) and disease present (illness positive).

The assumptions for using a chi-square test are shown in Box 7.2.

Box 7.2 Assumptions for using chi-square tests

The assumptions that must be met when using a chi-square test are that:

- each observation must be independent
- each participant is represented in the table once only
- 80% of the expected cell frequencies should exceed 5 and all expected cell frequencies should exceed 1

A major assumption of chi-square tests is independence, that is each participant must be represented in the analysis once only. Thus, if repeat data have been collected, for example if data have been collected from hospital inpatients and some patients have been re-admitted, a decision must be made about which data, for example, from the first admission or the last admission, are used in the analyses.

The expected frequency in each cell, which is discussed later in this chapter, is an important concept in determining *P* values and deciding the validity of a chi-square test. For each cell, a certain number of participants would be expected given the frequencies of each of the characteristics in the sample.

When a chi-square test is requested, most statistics programs provide a number of chi-square values on the output. The chi-square statistic that is conventionally used depends on both the sample size and the expected cell counts as shown in Table 7.4. However, these guidelines are quite conservative and if the result from a Fisher's exact test is available, it could be used in

Table 7.4 Type and application of chi-square tests

Statistic	Application
Pearsons' chi-square	Used when the sample size is very large, say over 1000
Continuity correction	Applied to 2 × 2 tables only and is an approximation to Pearson's for a smaller sample size, say less than 1000
Fisher's exact test	Must always be used when one or more cells in a 2 × 2 table have a small expected number of cases
Linear-by-linear	Used to test for a trend in the frequency of the outcome across an ordered exposure variable

all situations because it is a gold standard test, whereas Pearson's chi-square and the continuity correction tests are approximations. Fisher's exact test is generally printed for 2 × 2 tables and, depending on the program used, may also be produced for crosstabulations larger than 2 × 2. The linear-by-linear test is most appropriate in situations in which an ordered exposure variable has three or more categories and the outcome variable is binary.

As in all analyses, it is important to identify which variable is the outcome variable and which variable is the explanatory variable. This is important for setting up the crosstabulation table to display the percentages that are appropriate for answering the research question. This can be achieved by either:

- entering the explanatory variable in the rows, the outcome in the columns and using row percentages, or
- entering the explanatory variable in the columns, the outcome in the rows and using column percentages

A table set up in either of these ways will display the per cent of participants with the outcome of interest in each of the explanatory variable groups. In most study designs, the outcome is a disease and the explanatory variable is an exposure or an experimental group. However, in case–control studies in which cases are selected on the basis of their disease status, the disease may be treated as the explanatory variable and the exposure as the outcome variable.

Research question

The data set **surgery.sav** contains data from babies who were admitted to hospital for surgery. This sample was not selected randomly and therefore only percentages will apply and the terms incidence and prevalence cannot be used. However, chi-square tests are valid to assess whether there are any between-group differences in the proportion of babies with certain characteristics.

Question:	Are males who are admitted for surgery more likely than females to have been born prematurely?
Null hypothesis:	That the proportion of males in the premature group is equal to the proportion of females in the premature group.
Variables:	Outcome variable = prematurity (categorical, two levels) Explanatory variable = gender (categorical, two levels)

The command sequence to obtain a crosstabulation and chi-square test is shown in Box 7.3.

Box 7.3 SPSS commands to obtain a chi-square test

SPSS Commands

surgery – SPSS Data Editor

Analyze → Descriptive Statistics → Crosstabs

- *Crosstabs*
  - *Highlight Gender recoded and click into Row(s)*
  - *Highlight Prematurity and click into Column(s)*
  - *Click Statistics*
- *Crosstabs: Statistics*
  - *Tick Chi-square, click Continue*
- *Crosstabs*
  - *Click Cells*
- *Crosstabs: Cell Display*
  - *Counts: tick Observed (default),*
  - *Percentages: tick Row*
  - *Click Continue*
- *Crosstabs*
  - *Click OK*

Crosstabs

Gender Re-coded * Prematurity Crosstabulation

			Prematurity		
			Premature	**Term**	**Total**
Gender re-coded	Male	Count	33	49	82
		% within gender re-coded	40.2%	59.8%	100.0%
	Female	Count	12	47	59
		% within gender re-coded	20.3%	79.7%	100.0%
Total		Count	45	96	141
		% within gender re-coded	31.9%	68.1%	100.0%

Chi-Square Tests

	Value	***df***	**Asymp. sig. (two-sided)**	**Exact sig. (two-sided)**	**Exact sig. (one-sided)**
Pearson chi-square	6.256[b]	1	0.012		
Continuity correction[a]	5.374	1	0.020		
Likelihood ratio	6.464	1	0.011		
Fisher's exact test				0.017	0.009
Linear-by-linear association	6.212	1	0.013		
N of valid cases	141				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 18.83.

The first Crosstabulation table shows that the two variables each have two levels to create a 2 × 2 table with four cells. The table shows that 40.2% of males in the sample were premature compared with 20.3% of females, that is the rate of prematurity in the males is almost twice that in the females.

Chi-square values are calculated from the number of observed and expected frequencies in each cell of the crosstabulation. The observed numbers are the numbers shown in each cell of the crosstabulation. The expected number for each cell is calculated as

Row total × Column total/Grand total

For cell a in Table 7.3, the expected number is $((a + b) \times (a + c))/\text{Total}$

The above formula is an estimate of how many cases would be expected in any one cell given the frequencies of the outcome and the exposure in the sample. The Pearson chi-square value is then calculated by the following summation from all cells:

$$\text{Chi-square value} = \frac{\Sigma(\text{Observed count} - \text{Expected count})^2}{\text{Expected count}}$$

The continuity corrected chi-square is calculated in a similar way but with a correction made for a smaller sample size. Obviously, if the observed and expected values are similar, then the chi-square value will be close to zero and therefore will not be significant. The more different the observed and expected values are from one another, the larger the chi-square value becomes and the more likely the P value will be significant.

In the Crosstabulation, the smallest cell has an observed count of 12. The expected number for this cell is 59 × 45/141, or 18.83 as shown in the footnote of the Chi-Square Tests table.

In the Chi-Square Tests table, the continuity correction chi-square of 5.374 is conventionally used because the sample size is only 141 children. This value indicates that the difference in rates of prematurity between the genders is statistically significant at $P = 0.02$. This result would be reported as 'there was a significant difference in prematurity between males and females (40.2% vs 20.3%, $P = 0.02$)'.

Confidence intervals

When between-group differences are compared, the summary percentages are best shown with 95% confidence intervals. As discussed in Chapter 3, it is useful to include the 95% confidence intervals when results are shown as figures because the degree of overlap between them provides an approximate significance of the differences between groups.

Many statistics programs do not provide confidence intervals around frequency statistics. However, 95% confidence intervals can be easily computed using an Excel spreadsheet. The standard error around a proportion is calculated as $\sqrt{[p(1-p)/n]}$ where p is the proportion expressed as a decimal number and n is the number of cases in the group from which the proportion is calculated. The standard error around a proportion is rarely reported but is commonly converted into a 95% confidence interval which is $p \pm (\text{SE} \times 1.96)$.

An Excel spreadsheet in which the percentage is entered as its decimal equivalent in the first column and the number in the group is entered in the second column can be used to calculate confidence intervals as shown in Table 7.5.

Table 7.5 Excel spreadsheet to compute 95% confidence intervals around proportions

	Proportion	*N*	SE	Width	CI lower	CI upper
Male	0.402	82	0.054	0.106	0.296	0.508
Female	0.203	59	0.052	0.103	0.100	0.306

The formula for the standard error (SE) is entered into the formula bar of Excel as sqrt $(p \times (1 - p)/n)$ and the formula for the width of the confidence interval is entered as $1.96 \times \text{SE}$. This width, which is the dimension of the 95% confidence interval that is entered into SigmaPlot to draw bar charts with error bars, can then be both subtracted and added to the proportion to calculate the 95% confidence interval values shown in the last two columns of Table 7.5.

The calculations are undertaken in proportions (decimal numbers) but are easily converted back to percentages by moving the decimal point two places to the right. Using the converted values, the result could be reported as 'the percentage of male babies born prematurely was 40.2% (95% CI 29.6 to 50.8%). This was significantly higher than the percentage of female babies born prematurely which was 20.3% (95% CI 10.0 to 30.6%) ($P = 0.02$)'. The P value of 0.02 for this comparison is derived from the Chi-Square Tests table.

Creating a figure using SigmaPlot

The summary statistics from Table 7.5 can be entered into SigmaPlot by first using the commands *File* → *New* and then entering the percentages in column 1 and the width of the confidence interval, also converted to a percentage in column 2.

Column 1	Column 2
40.2	10.6
20.3	10.3

The SigmaPlot commands for plotting these summary statistics as a figure are shown in Box 7.4.

Box 7.4 SigmaPlot commands to draw simple histograms

SigmaPlot Commands

Sigmaplot – [Data 1]
    Graph → Create Graph
Create Graph - Type
    Highlight Horizontal Bar Chart, click Next
Create Graph - Style
    Highlight Simple Error Bars, click Next
Create Graph – Error Bars
    Symbol Values = Worksheet Columns (default), click Next
Create Graph – Data Format
    Highlight Single X, click Next
Create Graph – Select Data
    Data for Bar = use drop box and select Column 1
    Data for Error = use drop box and select Column 2
    Click Finish

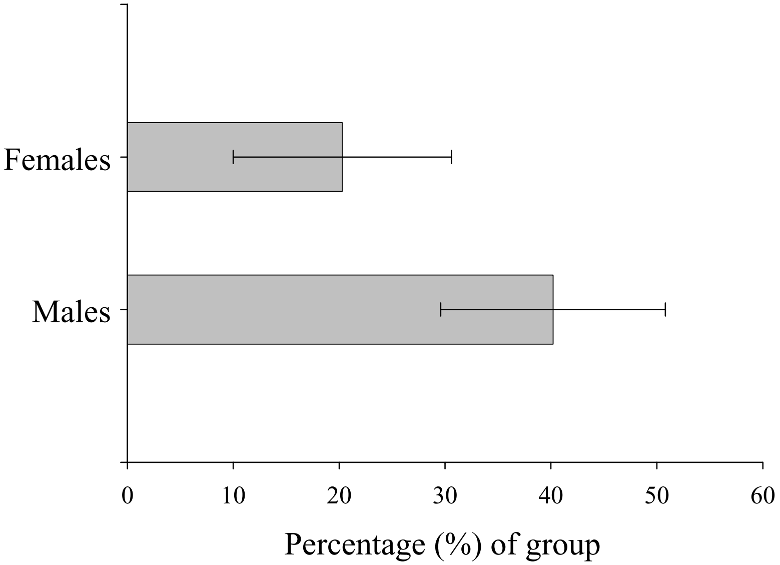

Figure 7.2 Per cent of male and female babies born prematurely.

The graph can then be customised using the options under *Graph → Properties* to produce Figure 7.2. The lack of overlap between the confidence intervals is an approximate indication of a statistically significant difference between the two groups.

2 × 3 chi-square tables

In addition to the common application of analysing 2 × 2 tables, chi-square tests can also be used for larger 2 × 3 tables in which one variable has two levels and the other variable has three levels.

Research question

Question:	Are the babies born in regional centres (away from the hospital or overseas) more likely to be premature than babies born in local areas?
Null hypothesis:	That the proportion of premature babies in the group born locally is not different to the proportion of premature babies in the groups born regionally or overseas.
Variables:	Place of birth (categorical, three levels and) prematurity (categorical, two levels)

In this research question, there is no clear outcome or explanatory variable because both variables in the analysis are characteristics of the babies. This type of question is asked when it is important to know about the inter-relationships between variables in the data set. If prematurity has an important association with place of birth, this may need to be taken into account in multivariate analyses.

The SPSS commands shown in Box 7.3 can be used with place of birth recoded entered into the rows, prematurity entered into the columns and row percentages requested.

Crosstabs

Place of birth (re-coded) * Prematurity Crosstabulation

			Prematurity		
			Premature	**Term**	**Total**
Place of birth (re-coded)	Local	Count	29	61	90
		% within place of birth (re-coded)	32.2%	67.8%	100.0%
	Regional	Count	6	27	33
		% within place of birth (re-coded)	18.2%	81.8%	100.0%
	Overseas	Count	5	4	9
		% within place of birth (re-coded)	55.6%	44.4%	100.0%
Total		Count	40	92	132
		% within place of birth (re-coded)	30.3%	69.7%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)
Pearson chi-square	5.170[a]	2	0.075
Likelihood ratio	5.146	2	0.076
Linear-by-linear association	0.028	1	0.866
N of valid cases	132		

[a] 1 cell (16.7%) has expected count less than 5. The minimum expected count is 2.73.

The row percentages in the Crosstabulation table show that there is a difference in the frequency of prematurity between babies born at different locations. The per cent of babies who are premature is 32.2% from local centres, 18.2% from regional centres and 55.6% from overseas centres. This difference in percentages fails to reach significance with a Pearson's chi-square value of 5.170 and a P value of 0.075. For tables such as this that are larger than 2 × 2, an exact chi-square test that is used when an expected count is low has to be requested and is not a default option (see next section).

In the crosstabulation, the absolute difference in per cent of premature babies between regional and overseas centres is quite large at 55.6% − 18.2%, or 37.4%. The finding of a non-significant P value in the presence of this large between-group difference could be considered a type II error as a consequence of the small sample size. In this case, the sample size is too small to demonstrate statistical significance when a large difference of 37.4% exists. If the sample size had been larger, then the P value for the same between-group difference would be significant. Conversely, the difference between the groups may have been due to chance and a larger sample size might show a smaller between-group difference.

A major problem with this analysis is the small numbers in some of the cells. There are only nine babies in the overseas group. The row percentages illustrate the problem that arises when some cells have small numbers. The five premature babies born overseas are 55.6% of their group because each baby is 1/9$^{\text{th}}$ or 11.1% of the group. When a group size is small, adding or losing a single case from a cell results in a large change in frequency statistics. Because of these small group sizes, the footnote in the Chi-Square Tests table indicates that one cell in the table has an expected count less than five.

Using the formula shown previously, the expected number of premature babies referred from overseas is 9 × 40/132 or 2.73. This minimum expected cell count is printed in the footnote below the Chi-Square Tests table. If a table has less than five expected observations in more than 20% of cells, the assumptions for the chi-square test are not met. The warning message suggests that the P value of 0.075 is unreliable and probably an overestimate of significance.

Cells with small numbers

Small cells cannot be avoided at times, for example when a disease is rare. However, cells and groups with small numbers are a problem in all types of analyses because their summary statistics are often unstable and difficult to interpret. When calculating a chi-square statistic, most packages will give a warning message when the number of expected cases in a cell is low.

Chi-square tests may be valid when the number of observed counts in a cell is zero as long as the expected number is greater than 5 in 80% of the cells and greater than 1 in all cells. If expected numbers are less than this, then an exact chi-square based on alternative assumptions can be used. An exact chi-square can be obtained for the 3 × 2 table above by clicking on the *Exact* button in the bottom left hand corner of the *Crosstabs* dialogue box. The following table is obtained when the Monte Carlo method of computing the exact chi-square is requested. The Monte Carlo P value is based on a random sample of a probability distribution rather than a chi-square distribution which is an approximation. When the Monte-Carlo option is selected, the P value will vary each time the test is run on the same data set because it is based on a random sample of probabilities.

The Chi-Square Tests table shows that the asymptotic significance value of $P = 0.075$ is identical to the exact significance value obtained previously i.e. $P = 0.075$. The two-sided test should be used because the direction of effect could have been either way, that is the proportion of premature babies could have been higher or lower in any of the groups.

An alternative to using exact methods is to merge the group with small cells with another group but only if the theory is valid. Alternatively, the group can be omitted from the analyses although this will reduce the generalisability of the results. It is usually sensible to combine groups when there are less than 10 cases in a cell. The number of viable cells for statistical analysis usually depends on sample size. As a rule of thumb, the maximum number of cells that can be tested using chi-square is the sample size divided by 10. Thus, a sample size of 160 could theoretically support 16 cells such as an 8 × 2 table, a 5 × 3 table or a 4 × 4 table. However, this relies on an even distribution of cases over the cells, which rarely occurs. In practice, the maximum number of cells is usually the sample size divided by 20. In this data set this would be 141/20 or approximately seven cells which would support a 2 × 2 or 2 × 3 table. These tables would be viable as long as no cell size is particularly small.

The pathway for analysing categorical variables when some cells have small numbers is shown in Figure 7.3.

Chi-Square Tests

				Monte Carlo sig. (two-sided)			Monte Carlo sig. (one-sided)		
					95% confidence interval			95% confidence interval	
	Value	*df*	Asymp. sig. (two-sided)	Sig.	Lower bound	Upper bound	Sig.	Lower bound	Upper bound
Pearson chi-square	5.170[a]	2	0.075	0.075[b]	0.070	0.081			
Likelihood ratio	5.146	2	0.076	0.100[b]	0.094	0.106			
Fisher's exact test	5.072			0.075[b]	0.070	0.081			
Linear-by-linear association	0.028[c]	1	0.866	0.879[b]	0.872	0.885	0.481[b]	0.472	0.491
N of valid cases	132								

[a] One cell (16.7%) has expected count less than 5. The minimum expected count is 2.73.

[b] Based on 10 000 sampled tables with starting seed 624387341.

[c] The standardized statistic is −0.168.

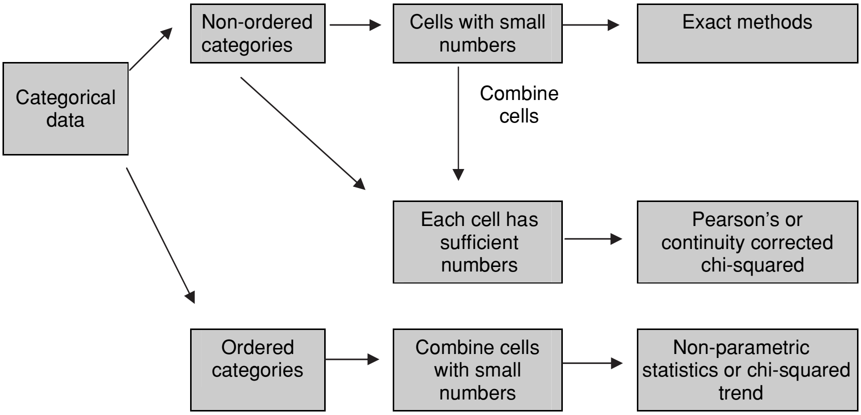
Categorical data
Non-ordered categories
Cells with small numbers
Exact methods
Combine cells
Each cell has sufficient numbers
Pearson's or continuity corrected chi-squared
Ordered categories
Combine cells with small numbers
Non-parametric statistics or chi-squared trend

Figure 7.3 Pathway for analysing categorical variables when some cells have small numbers.

Re-coding to avoid small cell numbers

Groups can easily be combined to increase cell size if the re-coding is intuitive. However, if two or more unrelated groups need to be combined, they could be described with a generic label such as 'other' if neither group is more closely related to one of the other groups in the analysis. In the data set **surgery.sav**, it makes sense to combine the regional group with the overseas group because both are distinct from the local group. The SPSS commands to transform a variable into a new variable were shown in Box 1.10 in Chapter 1 and can be used to transform place2 with three levels into a binary variable called place3 (local, regional/overseas). To ensure that all output is self-documented, it is important to label each new variable in Variable View after re-coding and to verify the frequencies of place3 using the commands shown in Box 1.9.

Frequencies

Place of Birth (Binary)

		Frequency	Per cent	Valid per cent	Cumulative per cent
Valid	Local	90	63.8	68.2	68.2
	Regional or overseas	42	29.8	31.8	100.0
	Total	132	93.6	100.0	
Missing	System	9	6.4		
Total		141	100.0		

Having combined the small overseas group of nine children with the regional group of 33 children, the new combined group has 42 children. The crosstabulation to answer the research question can then be repeated using the command sequence shown in Box 7.3 to compute a 2 × 2 table with the binary place of birth variable entered into the rows.

Crosstabs

Place of Birth (Binary) * Prematurity Crosstabulation

			Prematurity		
			Premature	**Term**	**Total**
Place of birth (binary)	Local	Count	29	61	90
		% within place of birth (binary)	32.2%	67.8%	100.0%
	Regional or overseas	Count	11	31	42
		% within place of birth (binary)	26.2%	73.8%	100.0%
Total		Count	40	92	132
		% within place of birth (binary)	30.3%	69.7%	100.0%

Chi-Square Tests

	Value	***df***	**Asymp. sig. (two-sided)**	**Exact sig. (two-sided)**	**Exact sig. (one-sided)**
Pearson chi-square	0.493[b]	1	0.482		
Continuity correction[a]	0.249	1	0.618		
Likelihood ratio	0.501	1	0.479		
Fisher's exact test				0.546	0.312
Linear-by-linear association	0.490	1	0.484		
N of valid cases	132				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 12.73.

The Crosstabulation shows that 32.2% of babies in the sample from local areas were premature compared to 26.2% of babies from regional centres or overseas. The Chi-Square Tests table shows the continuity corrected *P* value of 0.618 which is not significant. This value, which is very different from the *P* value of 0.075 for the 3 × 2 table, is more robust because all cells have adequate sizes. With the small cells combined with larger cells, the footnote shows that no cell has an expected count less than five and thus the assumptions for chi-square are met.

Using the Excel spreadsheet created previously in Table 7.5, the percentages can be added as proportions and the confidence intervals calculated as shown in Table 7.6.

Table 7.6 Excel spreadsheet to compute confidence intervals around proportions

	Proportion	*N*	SE	Width	CI lower	CI upper
Local	0.322	90	0.049	0.097	0.225	0.419
Regional or overseas	0.262	42	0.068	0.133	0.129	0.395

Presenting the results: crosstabulated information

When presenting crosstabulated information of the effects of explanatory factors for a report, journal article or presentation, it is appropriate to use tables with the outcome variable presented in the columns and the risk factors or explanatory variables presented in the rows as shown in Table 7.7.

The chi-square analyses show that the number of males and females referred for surgery is significantly different but that the per cent of premature babies from regional or overseas areas is not significantly different from the per cent of premature babies in the group born locally. The results of these analyses could be presented as shown in Table 7.7.

Table 7.7 Factors associated with prematurity in 141 children attending hospital for surgery

Risk factor	Per cent premature and 95% CI	*P* value
Male	40.2% (95% CI 29.6, 50.8)	0.02
Female	20.3% (95% CI 10.0, 30.6)	
Born in local area	32.2% (95% CI 22.5, 41.9)	0.62
Born in regional area or overseas	26.2% (95% CI 12.9, 39.5)	

The overlap of the 95% confidence intervals in this table is consistent with the *P* values and shows that there is only a minor overlap of 95% confidence intervals between genders but a large overlap of 95% confidence intervals between regions.

Differences in proportions

When comparing proportions between two groups, it can be useful to express the size of the absolute difference in proportions between the groups. A 95% confidence interval around this difference is invaluable in interpreting the significance of the difference because if the interval does not cross the line of no difference (zero value) then the difference between groups is statistically significant.

The Excel spreadsheet shown in Table 7.8 can be used to calculate the differences in proportions, the standard error around the differences and the width of the confidence intervals. The difference in proportions is calculated

Table 7.8 Excel spreadsheet to compute confidence intervals around a difference in proportions

	p1	n1	p2	n2	1–p1	1–p2	Difference	SE	Width	CI lower	CI upper
Gender	0.402	82	0.203	59	0.598	0.797	0.199	0.075	0.148	0.051	0.347
Place	0.322	90	0.262	42	0.678	0.738	0.06	0.084	0.164	−0.104	0.224

as $p_1 - p_2$ and the standard error of the difference as $\surd((p_1 \times (1 - p_1)/n_1) + (p_2 \times (1 - p_2)/n_2))$, where p_1 is the proportion and n_1 is the number of cases in one group and p_2 is the proportion and n_2 is the number of cases in the other group. The width of the confidence interval is calculated as before as SE × 1.96.

Presenting the results: differences in percentages

The results from the above analyses can be presented as shown in Table 7.9 as an alternative to the presentation shown in Table 7.7. In Table 7.7, the precision in both groups could be compared but Table 7.9 shows the absolute difference between the groups. This type of presentation is useful for example when comparing percentages between two groups that were studied in different time periods and the outcome of interest is the change over time.

Table 7.9 Risk factor for prematurity in 141 children attending for surgery

Risk factor	Per cent premature	Difference and 95% confidence interval	*P* value
Male	40.2%	19.9% (95% CI 5.1, 34.7)	0.02
Female	20.3%		
Born locally	32.2%	6.0% (95% CI −10.4, 22.4)	0.62
Born regionally/overseas	26.2%		

The 95% confidence interval for the difference between genders does not contain the zero value of no difference as expected because the P value is significant. On the other hand, the confidence interval for the difference between places of birth contains the zero value indicating there is little difference between groups and that the P value is not significant.

When using larger crosstabulations, such as 2 × 3 tables, it can be difficult to interpret the P value without further sub-analyses, as shown when answering the following research question.

Research question

Question: Are babies who are born prematurely more likely to require different types of surgical procedures than term babies?

Null hypothesis: That the proportion of babies who require each type of surgical procedure in the group born prematurely is the same as in the group of term babies.
Variables: Outcome variable = procedure performed (categorical, three levels)
Explanatory variable = prematurity (categorical, two levels)

In situations such as this where the table is 3 × 2 because the outcome has three levels, both the row and column cell percentages can be used to provide useful summary statistics for between-group comparisons. The commands shown in Box 7.3 can be used with prematurity as the explanatory variable entered in the rows and procedure performed as the outcome variable in the columns. In addition, the column percentages can be obtained by ticking the column option in *Cells*.

Crosstabs

Prematurity * Procedure Performed Crosstabulation

			Procedure performed			
			Abdominal	**Cardiac**	**Other**	**Total**
Prematurity	Premature	Count	9	23	13	45
		% within prematurity	20.0%	51.1%	28.9%	100.0%
		% within procedure performed	17.0%	41.1%	40.6%	31.9%
	Term	Count	44	33	19	96
		% within prematurity	45.8%	34.4%	19.8%	100.0%
		% within procedure performed	83.0%	58.9%	59.4%	68.1%
Total		Count	53	56	32	141
		% within prematurity	37.6%	39.7%	22.7%	100.0%
		% within procedure performed	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	***df***	**Asymp. sig. (two-sided)**
Pearson chi-square	8.718[a]	2	0.013
Likelihood ratio	9.237	2	0.010
Linear-by-linear association	6.392	1	0.011
N of valid cases	141		

[a] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 10.21.

The row percentages in the Crosstabulation show that fewer of the premature babies required abdominal procedures than the term babies (20.0% vs 45.8%) and that more of the premature babies had cardiac procedures than the term babies (51.1% vs 34.4%). In addition, more of the premature babies than the term babies had other procedures (28.9% vs 19.8%). The significance of these differences from the Chi-Square Tests table is $P = 0.013$. However, this P value does not indicate the specific between-group comparisons that are significantly different from one another. In practice, the P value indicates that there is a significant difference in percentages within the table but does indicate which groups are significantly different from one another. In this situation where there is no ordered explanatory variable, the linear by linear association has no interpretation.

The column percentages shown in the Crosstabulation table can be used to interpret the 2 × 2 comparisons. These percentages show that rates of surgery types in premature babies are abdominal vs cardiac surgery 17.0% vs 41.1%, abdominal vs other surgery 17.0% vs 40.6% and cardiac vs other surgery 41.1% vs 40.6%. To obtain P values for these comparisons, the *Data → Select Cases → If condition is satisfied* option can be used to select two groups at a time and compute three separate 2 × 2 tables. For the three comparisons above, this provides P values of 0.011, 0.031 and 1.0 respectively. Thus, the original P value from the 2 × 3 table was significant because the rate of prematurity was significantly lower in the abdominal surgery group compared to both the cardiac and other surgery groups. However, there was no significant difference between the cardiac vs other surgery group. This process of making multiple comparisons increases the chance of a type I error, that is finding a significant difference when one does not exist. A preferable method is to compute confidence intervals as shown in the Excel spreadsheet in Table 7.5 and then examine the degree of overlap. The computed intervals are shown in Table 7.10.

Table 7.10 Excel spreadsheet to compute confidence intervals around proportions

	Proportion	*N*	SE	Width	CI lower	CI upper
Abdominal-premature	0.17	53	0.052	0.101	0.069	0.271
Cardiac-premature	0.411	56	0.066	0.129	0.282	0.540
Other-premature	0.406	32	0.087	0.170	0.236	0.576
Abdominal-term	0.83	53	0.052	0.101	0.729	0.931
Cardiac-term	0.589	56	0.066	0.129	0.460	0.718
Other-term	0.594	32	0.087	0.170	0.424	0.764

The rates and their confidence intervals can then be plotted using SigmaPlot as shown in Box 7.5. The data sheet has the proportions and confidence interval widths converted into percentages for the premature babies in columns 1 and 2 and for the term babies in columns 3 and 4 as follows.

Column 1	Column 2	Column 3	Column 4
17.0	10.1	83.0	10.1
41.1	12.9	58.9	12.9
40.6	17.0	59.4	17.0

Box 7.5 SigmaPlot commands for plotting multiple bars

SigmaPlot Commands

```
SigmaPlot – [Data 1*]
        Graph → Create Graph
Create Graph - Type
        Highlight Horizontal Bar Chart, click Next
Create Graph - Style
        Highlight Grouped Error Bars, click Next
Create Graph – Error Bars
        Symbol Values = Worksheet Columns (default), click Next
Create Graph – Data Format
        Highlight Many X, click Next
Create Graph – Select Data
        Data for Set 1 = used drop box and select Column 1
        Data for Error 1 = used drop box and select Column 2
        Data for Set 2 = used drop box and select Column 3
        Data for Error 2 = used drop box and select Column 4
        Click Finish
```

Figure 7.4 shows clearly that the 95% confidence intervals of the bars for the per cent of the abdominal surgery group who are term or premature babies do not overlap either of the other groups and therefore the percentages are significantly different as described by the *P* values. The sample percentages of term and premature babies in the cardiac surgery and other procedure groups are almost identical as described by the *P* value of 1.0.

Larger chi-square tables

In addition to 2 × 2 and 2 × 3 tables, chi-square tests can also be used to analyse tables of larger dimensions as shown in the following research question. However, the same assumptions apply and the sample size should be sufficient to support the table without creating small cells with few expected counts.

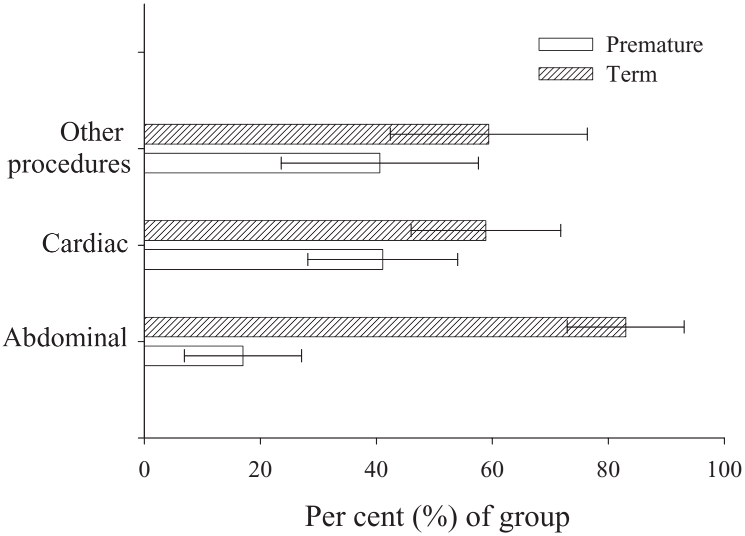

Figure 7.4 Percentage of surgical procedures in premature and term babies.

Research question

Question:	Do babies who have a cardiac procedure stay in hospital longer than babies who have other procedures?
Null hypothesis:	That length of stay is not different between children who undergo different procedures
Variables:	Outcome variable = length of stay (categorised into quintiles) Explanatory variable = procedure performed (categorical, three levels)

In the data set, length of stay is a right skewed continuous variable. As an alternative to using rank-based non-parametric tests, it is often useful to divide non-normally distributed variables such as this into categories. Box 7.6 shows the SPSS commands that can be used to divide length of stay into quintiles, that is five groups with approximately equal cell sizes.

Box 7.6 SPSS commands to categorise variables

SPSS Commands

surgery – SPSS Data Editor

Transform → Categorize Variables

Categorize Variables

Highlight Length of stay and click into 'Create Categories for' box

Enter the number 5 into the 'Number of categories' box

Click OK

Once this new variable is obtained, it should be labelled in the Variable View window, for example this variable has been labelled 'Length of stay quintiles'. The SPSS commands to obtain information about the sample size of each quintile and the range of values in each quintile band are shown in Box 7.7.

Box 7.7 SPSS commands to obtain statistics for each quintile

SPSS Commands

```
surgery – SPSS Data Editor
        Data → Split file
Split File
        Click option 'Organize output by groups'
        Highlight Length of stay quintiles and click into 'Groups based on'
        Click OK
surgery – SPSS Data Editor
        Analyze→ Descriptive Statistics →Descriptives
Descriptives
        Highlight Length of stay and click into Variable(s) box
        Click OK
```

Descriptives

Length of stay quintiles = 1

Descriptive Statistics[a]

	N	Minimum	Maximum	Mean	Std. deviation
Length of stay	25	0	18	13.52	4.556
Valid *N* (listwise)	25				

[a] Length of stay quintiles = 1.

Length of stay quintiles = 2

Descriptive Statistics[a]

	N	Minimum	Maximum	Mean	Std. deviation
Length of stay	29	19	22	20.86	1.060
Valid *N* (listwise)	29				

[a] Length of stay quintiles = 2.

Length of stay quintiles = 3

Descriptive Statistics[a]

	N	Minimum	Maximum	Mean	Std. deviation
Length of stay	26	23	30	26.96	2.720
Valid *N* (listwise)	26				

[a] Length of stay quintiles = 3.

Length of stay quintiles = 4

Descriptive Statistics[a]

	N	Minimum	Maximum	Mean	Std. deviation
Length of stay	26	31	44	39.31	3.813
Valid *N* (listwise)	26				

[a] Length of stay quintiles = 4.

Length of stay quintiles = 5

Descriptive Statistics[a]

	N	Minimum	Maximum	Mean	Std. deviation
Length of stay	26	45	244	90.65	52.092
Valid *N* (listwise)	26				

[a] Length of stay quintiles = 5.

The output shows the number of cases, the mean, and the minimum and maximum days of each quintile. This information is important for labelling the quintile groups in Variable View so that the output is self-documented. The information of quintile ranges is also important for describing the quintile values when reporting the results. The number of cases in some quintiles are unequal because there are some ties in the data.

The SPSS commands for obtaining crosstabulations shown in Box 7.3 can now be used to answer the research question. Before running the crosstabulation, the *Data → Split File* command needs to be reversed using the option *Analyze all cases, do not create groups* in *Split File*. In the crosstabulation, the procedure performed is entered into the rows as explanatory variable and length of stay quintiles are entered in the columns as the outcome variable. The row percentages are selected in *Cells*.

It is very difficult to interpret large tables such as this 3 × 5 table. The crosstabulation has 15 cells, each with fewer than 20 observed cases. Although some cells have only two or three cases, the Chi-Square Tests footnote shows that no cells have an expected number less than 5, so that the analysis and the P value are valid. Although the P value is significant at $P = 0.004$, no clear trends are apparent in the table. If the cardiac and abdominal patients are compared, the abdominal group has fewer babies in the lowest quintile and the cardiac group has slightly fewer babies in the highest quintile. In the group of babies who had other procedures, most babies are either in the lowest or in the highest quintiles of length of stay. Thus, the P value is difficult to interpret without any further sub-group analyses and the interpretation of the statistical significance of the results is difficult to communicate. Again, in a table such as this with a non-ordered explanatory variable, the linear-by-linear statistic has no interpretation and should not be used. A solution to removing small cells would be to divide length of stay into two groups only, perhaps above and below the median value or above and below a clinically

Procedure Performed * Length of Stay Quintiles Crosstabulation

			Length of stay quintiles					
			0–18 days	19–22 days	23–30 days	31–44 days	45–244 days	Total
Procedure performed	Abdominal	Count	2	11	15	11	9	48
		% within procedure performed	4.2%	22.9%	31.3%	22.9%	18.8%	100.0%
	Cardiac	Count	15	13	7	12	6	53
		% within procedure performed	28.3%	24.5%	13.2%	22.6%	11.3%	100.0%
	Other	Count	8	5	4	3	11	31
		% within procedure performed	25.8%	16.1%	12.9%	9.7%	35.5%	100.0%
Total		Count	25	29	26	26	26	132
		% within procedure performed	18.9%	22.0%	19.7%	19.7%	19.7%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)
Pearson chi-square	22.425[a]	8	0.004
Likelihood ratio	24.341	8	0.002
Linear-by-linear association	0.676	1	0.411
N of valid cases	132		

[a] 0 cells (0.0%) has expected count less than 5. The minimum expected count is 5.87.

important threshold, and to examine the per cent of babies in each procedure group who have long or short stays.

Chi-square trend test for ordered variables

Chi-square trend tests, which in SPSS are called linear-by-linear associations, work well when the exposure variable can be categorised into ordered groups, such as quintiles for length of stay, and the outcome variable is binary. The linear-by-linear statistic then indicates whether there is a trend for the outcome to increase or decrease as the exposure increases.

Research question

Question:	Is there a trend for babies who stay longer in hospital to have a higher infection rate?
Null hypothesis:	That infection rates do not change with length of stay
Variables:	Outcome variable = infection (categorical, two levels) Explanatory/exposure variable = length of stay (categorised into quintiles, ordered)

In this research question, it makes sense to test whether there is a trend for the per cent of babies with infection to increase significantly with an increase in length of stay. The SPSS commands shown in Box 7.3 can be used with length of stay quintiles in the rows, infection in the columns and the row percentages requested.

Crosstabs

Length of Stay Quintiles * Infection Crosstabulation

			Infection		
			No	Yes	Total
Length of stay quintiles	0–18 days	Count	19	6	25
		% within length of stay quintiles	76.0%	24.0%	100.0%
	19–22 days	Count	21	8	29
		% within length of stay quintiles	72.4%	27.6%	100.0%

Continued

			Infection		
			No	Yes	Total
	23–30 days	Count	17	9	26
		% within length of stay quintiles	65.4%	34.6%	100.0%
	31–44 days	Count	12	14	26
		% within length of stay quintiles	46.2%	53.8%	100.0%
	45–244 days	Count	11	15	26
		% within length of stay quintiles	42.3%	57.7%	100.0%
Total		Count	80	52	132
		% within length of stay quintiles	60.6%	39.4%	100.0%

Chi-Square Tests

	Value	df	Asymp. sig. (two-sided)
Pearson chi-square	10.344[a]	4	0.035
Likelihood ratio	10.433	4	0.034
Linear-by-linear association	9.551	1	0.002
N of valid cases	132		

[a] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 9.85.

The Crosstabulation table shows that the per cent of children with infection increases with length of stay quintile, from 24.0% in the lowest length of stay quintile group to 57.7% in the highest quintile group. The Pearson chi-square indicates that there is a significant difference in percentages between some groups in the table with $P = 0.035$. From this, it can be inferred that the lowest rate of infection in the bottom quintile is significantly different from the highest rate in the top quintile but not that any other rates are significantly different from one other. More usefully, the linear-by-linear association indicates that there is a significant trend for infection to increase with length of stay at $P = 0.002$.

Presenting the results

When presenting the effects of an ordered exposure variable on several outcomes in a scientific table, the exposure groups are best shown in the columns and the outcomes in the rows. This is the reverse presentation to Table 7.9. Using this layout the per cent of babies in each exposure group can be compared across a line of the table. The data from the Crosstabulation above can be presented as shown in Table 7.11. If other outcomes associated with length of stay were also investigated, further rows could be added to the table.

Table 7.11 Rates of infection by length of stay

	Length of stay in quintiles						
	1	**2**	**3**	**4**	**5**		***P* value**
Range (days)	**0–18**	**19–22**	**23–30**	**31–44**	**45–244**	***P* value**	**for trend**
Number in group	25	29	26	26	26		
Percentage with infection	24.0%	27.6%	34.6%	53.8%	57.7%	0.035	0.002

To obtain a graphical indication of the magnitude of the trend across the data, a clustered bar chart can be requested using the SPSS commands shown in Box 7.8. If the number of cases in each group is unequal, as in this data set, then percentages rather than numbers must be selected in the *Bars Represent* option so that the height of each bar is standardised for the different numbers in each group and can be directly compared.

Box 7.8 SPSS commands to obtain a clustered bar chart

SPSS Commands

```
surgery – SPSS Data Editor
        Graphs →Bar
Bar Charts
        Click Clustered, click Define
Define Clustered Bar: Summaries for Groups of Cases
        Bars Represent: Tick % of cases box
        Highlight Infection and click into Category Axis
        Highlight Length of stay quintiles and click into Define Clusters by
        Click Options
Options
        Omit default check for Display groups defined by missing variables
           Click Continue
Define Clustered Bar: Summaries for Groups of Cases
        Click OK
```

In Figure 7.5, the group of bars on the left hand side of the graph shows the decrease in the per cent of babies who did not have infection across length of stay quintiles. The group of bars on the right hand side shows the complement of the data, that is the increase across quintiles of the per cent of babies who did have infection. A way of presenting the data to answer the research question would be to draw a bar chart of the per cent of children with infection only as shown on the right hand side of Figure 7.5. This chart can be drawn in SigmaPlot using the commands shown in Box 7.4 with a vertical bar chart rather than a horizontal bar chart selected. Using the SigmaPlot commands *Statistics → Linear Regression → All data in plot* will provide a plot that is more useful for presenting the results in that a trend line across exposures is shown as in Figure 7.6.

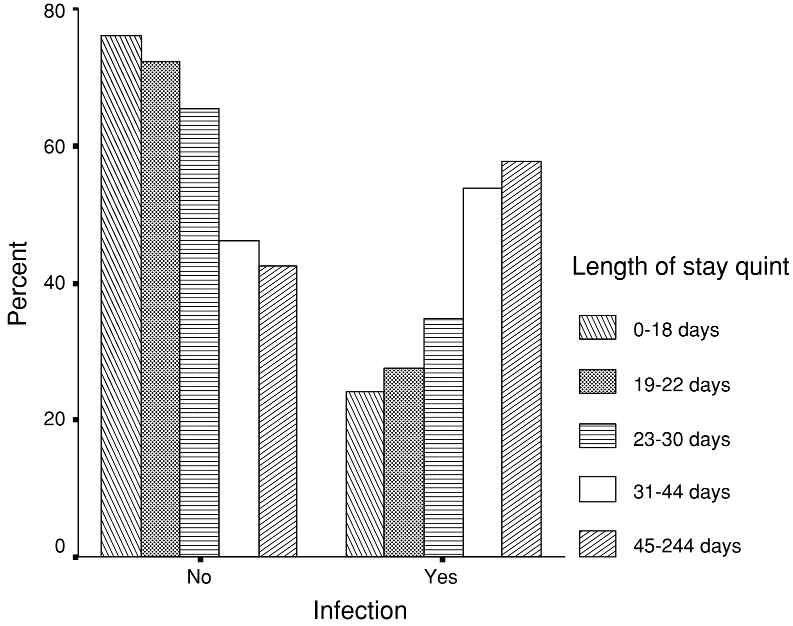

Figure 7.5 Length of stay quintiles for babies by infection status.

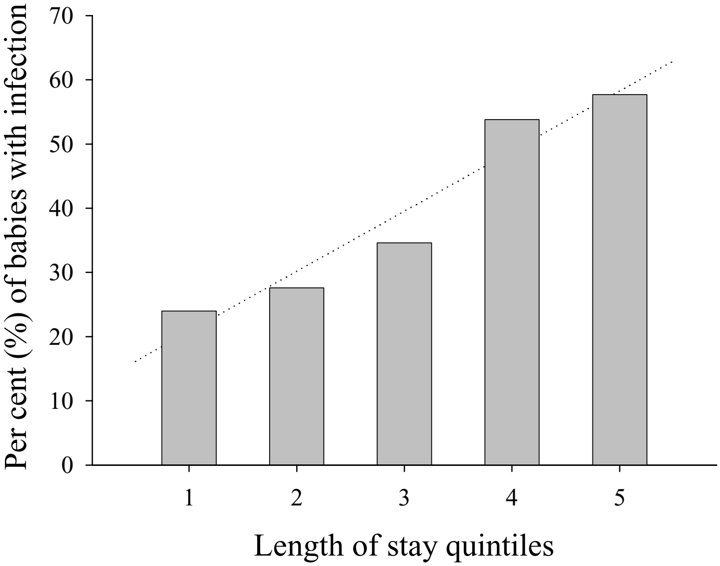

Figure 7.6 Rate of infection across length of stay quintiles.

Number needed to treat

In interpreting the results from clinical trials, clinicians are often interested in how many patients need to be administered a treatment to prevent one adverse event. This statistic, which is called number needed to treat (NNT), can be calculated from clinical studies in which the effectiveness of an intervention is compared in two groups, for example a standard treatment group and a new treatment group. For 2 × 2 crosstabulations, a chi-square test is used to indicate significance between the groups or a difference in proportions is used to indicate whether the new treatment group has a significantly lower rate of adverse events than the standard treatment group. However, in clinical situations, these statistics, which describe the general differences between two groups, may not be the major results of interest. In a clinical setting, the statistic NNT provides a number that can be directly applied to individual patients and may therefore be more informative.

To calculate NNT, two categorical variables each with two levels are required in order to compute a 2 × 2 crosstabulation. One variable must indicate the presence or absence of the adverse event, for example, an outcome such as death or disability, and the other variable must indicate group status (exposure), for example whether patients are in the intervention or control group.

The file **therapy.sav** contains data for 200 patients, half of whom were randomised to receive standard therapy and half of whom were randomised to receive a new therapy. The two outcomes that have been collected are the presence or absence of stroke and the presence or absence of disability. Each outcome variable is a binary yes/no response. Using the commands shown in Box 7.3, the following 2 × 2 tables for each outcome can be obtained. To calculate NNT, the outcome is entered as the rows, the treatment group is entered in the columns and column percentages are requested.

Crosstabs

Stroke * Treatment Group Crosstabulation

			Treatment group		
			New therapy	**Standard treatment**	**Total**
Stroke	No complications	Count	85	79	164
		% within treatment group	85.0%	79.0%	82.0%
	Stroke	Count	15	21	36
		% within treatment group	15.0%	21.0%	18.0%
Total		Count	100	100	200
		% within treatment group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Pearson chi-square	1.220[b]	1	0.269		
Continuity correction[a]	0.847	1	0.357		
Likelihood ratio	1.224	1	0.269		
Fishers exact test				0.358	0.179
Linear-by-linear association	1.213	1	0.271		
N of valid cases	200				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 18.00.

The first Crosstabulation shows that the rate of stroke is 15% in the new treatment group compared to 21.0% in the standard treatment group. The Chi-Square Tests table shows the continuity corrected chi-square value with $P = 0.357$ which indicates that this difference in rates is not statistically significant. However, statistical significance, which depends largely on sample size, may not be of primary interest in a clinical setting.

From the table, NNT is calculated from the absolute risk reduction (ARR), which is simply the difference in the per cent of patients with the outcome of interest between the groups. From the Crosstabulation for stroke:

$$\text{ARR} = 21.0\% - 15.0\% = 6.0\%$$

ARR is then converted to a proportion, which in decimal format is 0.06, and the reciprocal is taken to obtain NNT:

$$\text{NNT} = 1/\text{ARR} = 1/0.06 = 16.67$$

Obviously, NNT is always rounded to the nearest whole number. This indicates that 17 people will need to receive the new treatment to prevent one extra person from having a stroke.

Crosstabs

Disability * Treatment Group Crosstabulation

			Treatment group		
			New therapy	Standard treatment	Total
Disability	No disability	Count	82	68	150
		% within treatment group	82.0%	68.0%	75.0%
	Disability	Count	18	32	50
		% within treatment group	18.0%	32.0%	25.0%
Total		Count	100	100	200
		% within treatment group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Pearson chi-square	5.227[b]	1	0.022		
Continuity correction[a]	4.507	1	0.034		
Likelihood ratio	5.281	1	0.022		
Fishers exact test				0.033	0.017
Linear-by-linear association	5.201	1	0.023		
N of valid cases	200				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 25.00.

The second Crosstabulation shows that the rate of disability is 18% in the new treatment group compared to 32.0% in the standard treatment group. The continuity corrected chi-square value with $P = 0.034$ shows that this new treatment achieves a significant reduction in rate of disability. The calculation of NNT is as follows:

$$\text{ARR} = 32.0\% - 18.0\% = 14.0\%$$

$$\text{NNT} = 1/\text{ARR} = 1/0.14 = 7.14$$

This indicates that seven people will need to receive the new treatment to prevent one extra person having a major disability. The larger the difference between groups as shown by a larger ARR, the fewer the number of patients who need to receive the treatment to prevent occurrence of one additional adverse event. Methods for calculating confidence intervals for NNT, which must be a positive number, are reported in the literature[2].

If nothing goes wrong, is everything OK?

Occasionally in clinical trials there may be no events in one group. If the *Crosstabs* procedure is repeated again, with the variable indicating survival entered as the outcome in the rows, the following table is produced.

Crosstabs

Death * Treatment Group Crosstabulation

			Treatment group		
			New therapy	Standard treatment	Total
Death	Survived	Count	100	92	192
		% within treatment group	100.0%	92.0%	96.0%
	Died	Count	0	8	8
		% within treatment group	0.0%	8.0%	4.0%
Total		Count	100	100	200
		% within treatment group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Pearson chi-square	8.333[b]	1	0.004		
Continuity correction[a]	6.380	1	0.012		
Likelihood ratio	11.424	1	0.001		
Fishers exact test				0.007	0.003
Linear-by-linear association	8.292	1	0.004		
N of valid cases	200				

[a] Computed only for a 2 × 2 table.

[b] 2 cells (50.0%) have expected count less than 5. The minimum expected count is 4.00.

When no adverse events occur in a group, as for deaths in the new treatment group this does not mean that no deaths will ever occur in patients who receive the new treatment. One way to estimate the proportion of patients in this group who might die is to calculate the upper end of the confidence interval around the zero percentage. To compute a confidence interval around a percentage that is less than 1% requires exact methods based on a binomial distribution. However, a rough estimate of the upper 95% confidence interval around a zero percentage is $3/n$ where n is the number of participants in the group. From the Crosstabulation, the upper 95% confidence interval around no deaths in the new therapy group would then be 3/100, or 3%. This is an approximate calculation only and may yield a conservative estimate. For more accurate estimates, Web programs are available (see Useful Web sites).

Paired categorical variables

Paired categorical measurements taken from the same participants on two occasions or matched categorical data collected in matched case – control studies must be analysed using tests for repeated data.

The measurements collected in these types of study designs are not independent and therefore chi-square tests cannot be used because the assumptions would be violated. In this situation, McNemar's test is used to assess whether there is a significant change in proportions over time for paired data or whether there is a significant difference in proportions between matched cases and controls. In this type of analysis, the outcome of interest is the within-person changes or the within-pair differences and there are no explanatory variables.

Research question

The file **health-camp.sav** contains the data from 86 children who attended a camp to learn how to self-manage their illness. The children were asked whether they knew how to manage their illness appropriately and whether they knew when to use their rescue medication appropriately at both the start and completion of the camp.

Question:	Did attendance at the camp increase the number of children who knew how to manage their illness appropriately?
Null hypothesis:	That there was no change in children's knowledge of illness management between the beginning and completion of the health camp.
Variables:	Appropriate knowledge (categorical, binary) at the beginning and completion of the camp.

In this research question the explanatory variable is time which is built into the analysis method and knowledge at both Time 1 and Time 2 are the outcome variables.

The assumptions for using paired categorical tests are shown in Box 7.9.

Box 7.9 Assumptions for a paired McNemar's test

For a paired McNemar's test the following assumptions must be met:
- the outcome variable has a categorical scale
- each participant is represented in the table once only
- the difference between the paired proportions is the outcome of interest

The relation between the measurements is summarised using a paired 2 × 2 contingency table and McNemar's test can be obtained using the commands shown in Box 7.10.

Box 7.10 SPSS commands to obtain McNemar's test

SPSS Commands

health-camp – SPSS Data Editor
    Analyze → Descriptive Statistics → Crosstabs
Crosstabs
    Highlight Knowledge-Time1 and click into Row(s)
    Highlight Knowledge-Time2 and click into Column(s)
    Click on Statistics
Crosstabs: Statistics
    Tick McNemar, click Continue
Crosstabs
    Click on Cells
Crosstabs: Cell Display
    Tick Observed under Counts (default), tick Total under Percentages
    Click Continue
Crosstabs
    Click OK

Crosstabs

Knowledge–Time1 * Knowledge–Time2 Crosstabulation

			Knowledge–Time2		
			No	**Yes**	**Total**
Knowledge–Time1	No	Count	27	29	56
		% of total	31.4%	33.7%	65.1%
	Yes	Count	6	24	30
		% of total	7.0%	27.9%	34.9%
Total		Count	33	53	86
		% of total	38.4%	61.6%	100.0%

Chi-Square Tests

	Value	**Exact sig. (two-sided)**
McNemar test		0.000[a]
N of valid cases	86	

[a] Binomial distribution used.

In the Crosstabulation, the total column and total row cells indicate that 34.9% of children had appropriate knowledge at the beginning of the camp (Yes at Time 1) and 61.6% at the end of the camp (Yes at Time 2). More importantly, the internal cells of the table show that 31.4% of children did not have appropriate knowledge on both occasions and 27.9% did have appropriate knowledge on both occasions. The percentages also show that 33.7% of children improved their knowledge (i.e. went from No at Time 1 to Yes at Time 2) and only 7.0% of children reduced their knowledge (i.e. went from Yes at Time 1 to No at Time 2). The Chi-Square Tests table shows a McNemar *P* value of <0.0001 indicating a significant increase in the proportion of children who improved their illness management knowledge.

When reporting paired information, summary statistics that reflect how many children improved their knowledge compared to how many children reduced their knowledge are used. This difference in proportions with its 95% confidence interval can be calculated using Excel.

In computing these statistics from the Crosstabulation table, the concordant cells are not used and only the information from the discordant cells is of interest as shown in Table 7.12. In Table 7.12, the two concordant cells (*a* and *d*) show the number of children who did or did not have appropriate knowledge at both the beginning and end of the camp. The two discordant cells (*b* and *c*) show the number of children who changed their knowledge status in either direction between the two occasions.

The counts in the discordant cells are used in calculating the change as a proportion and the SE of difference from the cell counts as follows:

Table 7.12 Presentation of data showing discordant cells

	No at end of camp	Yes at end of camp	Total
No at beginning of camp	27 *a*	29 *b*	56
Yes at beginning of camp	*c* 6	*d* 24	30
Total	33	53	*n* 86

$$\text{Difference in proportions} = (b - c)/n$$

$$\text{SE of difference} = 1/n \times \surd(b + c - ((b - c)^2/n))$$

For large sample sizes, the 95% confidence interval around the difference in proportions is calculated as 1.96 × SE. These statistics can be computed using the discordant cell counts in an Excel spreadsheet as shown in Table 7.13 and the proportions for appropriate knowledge at the beginning of the camp (Yes at Time1) and end of the camp (Yes at Time 2). The table shows that the increase in knowledge converted back to a percentage is 26.7% (95% CI 14.5, 39.0). The 95% confidence interval does not cross the zero line of no difference which reflects the finding that the change in proportions is statistically significant.

Table 7.13 Excel spreadsheet to compute differences for paired data

	p2 Yes-Time2	p1 Yes-Time1	Total N	Difference	SE	95% CI width	CI lower	CI upper
Knowledge	0.616	0.349	86	0.267	0.062	0.122	0.145	0.390

A second outcome that was measured in the study was whether children knew when to use their rescue medication appropriately. The commands shown in Box 7.10 can be used to obtain a McNemar's test for this outcome by entering medication-time 1 into the rows and medication-time 2 into the columns of the crosstabulation. Again, only the total percentages are requested.

Crosstabs

Medication–Time1 * Medication–Time2 Crosstabulation

			Medication–Time2		
			No	**Yes**	**Total**
Medication–Time1	NO	Count	17	13	30
		% of total	19.8%	15.1%	34.9%
	Yes	Count	11	45	56
		% of total	12.8%	52.3%	65.1%
Total		Count	28	58	86
		% of total	32.6%	67.4%	100.0%

Chi-Square Tests

	Value	Exact sig. (two-sided)
McNemar test		0.839[a]
N of valid cases	86	

[a] Binomial distribution used.

The percentages in the discordant cells indicate a small increase in knowledge of 15.1% to 12.8%, or 2.3%. The Chi-Square Tests table shows that this difference is not significant with a *P* value of 0.839. The Excel spreadsheet shown in Table 7.13 can be used to obtain the paired difference and its 95% confidence interval as proportions as shown in Table 7.14. The increase in knowledge is 2.3% (95% CI –8.8%, 13.5%). The 95% confidence interval crosses the zero line of no difference reflecting the finding that the change in proportions is not statistically significant.

Table 7.14 Excel spreadsheet to compute differences for paired data

	p2 Yes-Time2	p1 Yes-Time1	Total N	Difference	SE	95% CI width	CI lower	CI upper
Medication	0.674	0.651	86	0.023	0.057	0.112	−0.088	0.135

Presenting the results

The analyses show that the number of children who knew how to manage their illness appropriately increased significantly and that the number of children who knew when to use their rescue medication increased slightly but not significantly on completion of the camp. These results could be presented as shown in Table 7.15. By reporting the per cent of children with knowledge on both occasions, the per cent increase and the *P* value, all information that is relevant to interpreting the findings is included.

Table 7.15 Changes in knowledge of management and medication use in 86 children following camp attendance

	Knowledge at entry	Knowledge on leaving	% increase and 95% CI	*P* value
Management	34.9%	61.6%	26.7% (14.5, 39.0)	<0.0001
Medication use	65.1%	67.4%	2.3% (−8.8, 13.5)	0.84

Notes for critical appraisal

There are many ways in which crosstabulations can be used and chi-square values can be computed. These values often depend on the sample size and can be biased by cells with only a small number of expected counts. When critically appraising an article that presents categorical data analysed using univariate statistics or crosstabulations, it is important to ask the questions shown in Box 7.11.

Box 7.11 Questions for critical appraisal

The following questions should be asked when appraising published results from analyses in which crosstabulations are used:

- Has any participant been included in an analysis more than once?
- Have the correct terms to describe rates or proportions been used?
- Is the correct chi-square value presented?
- Could any small cells have biased the *P* value?
- Are percentages reported so that the size of the difference is clear?
- Have 95% confidence intervals for percentages been reported?
- If two groups are being compared, is the difference between them shown?
- If the exposure variable is ordered, is a trend statistic reported?
- Is it clear how any 'missing data' have influenced the results?
- Are the most important findings reported as a figure?
- If the results of a trial to test an intervention are being reported, is NNT presented?
- If the data are paired, has a paired statistical test been used?

References

1. Bland M. An introduction to medical statistics (2nd edition). Oxford, UK: Oxford University Press, 1996; p. 3.
2. Altman DG. Confidence intervals for number needed to treat. BMJ 1998; 317: 1309–1312.

CHAPTER 8
Categorical variables: risk statistics

Clinicians have a good intuitive understanding of risk and even of a ratio of risks. Gamblers have a good intuitive understanding of odds. No one (with the possible exception of certain statisticians) intuitively understands a ratio of odds.[1]

Objectives

The objectives of this chapter are to explain how to:

- decide whether odds ratio or relative risk is the appropriate statistic to use
- use logistic regression to compute adjusted odds ratios
- report and plot unadjusted and adjusted odds ratios
- change risk estimates to protection and vice versa
- calculate 95% confidence intervals around estimates of risk
- critically appraise the literature in which estimates of risk are reported

Chi-square tests indicate whether two binary variables such as an exposure and an outcome measurement are independent or are significantly related to each other. However, apart from the P value, chi-square tests do not provide a statistic for describing the strength of the relationship. Two statistics that are useful for measuring the magnitude of the association between two binary variables measured in a 2×2 table are the odds ratio or a relative risk. Both of these statistics are estimates of risk and, as such, describe the probability that people who are exposed to a certain factor will have a disease compared to people who are not exposed to the same factor.

The choice of using an odds ratio or relative risk depends on both the study design and whether bivariate or multivariate analyses are required. Relative risk is an appropriate risk statistic to use when the sample has been selected randomly, such as in a cohort or cross-sectional study, and when only bivariate analyses are required. Odds ratios have the advantage that they can be used in any study design, including case–control studies in which the proportion of cases is unlikely to be representative of the proportion in the population, and they can be adjusted for the effects of other confounders in multivariate analyses.

Both odds ratio and relative risk are widely used in epidemiological and clinical research to describe the risk of people having a disease (or an outcome) in the presence of an exposure, which may be an environmental factor, a treatment or any other type of explanatory factor. In case–control studies, odds ratio is used to measure the odds that a case has been exposed compared to the odds that a control has had the same exposure.

The way in which tables to calculate risk statistics are classically set up in the clinical epidemiology textbooks is shown in Table 8.1.

Table 8.1 Table to measure the relation between a disease and an exposure

	Disease present	Disease absent	Total
Exposure present	a	b	$a+b$
Exposure absent	c	d	$c+d$
Total	$a+c$	$b+d$	N

The odds ratio and relative risk compare the likelihood of an event occurring between two groups. The odds is a ratio of the probability of an event occurring to the probability of an event not occurring[2]. The odds ratio is calculated by comparing the odds of an event in one group (e.g. exposure present) to the odds of the same event in another group (e.g. exposure absent). From Table 8.1, the odds of the disease in the exposed group compared to the odds of the disease in the non-exposed group can be calculated as follows:

$$\text{Odds ratio (OR)} = (a/b)/(c/d) = (a \times d)/(b \times c)$$

This calculation shows why an odds ratio is sometimes called a ratio of cross-products. On the other hand, relative risk compares the conditional probability of the event occurring in the exposed and non-exposed groups and is calculated as follows:

$$\text{Relative risk (RR)} = \frac{a/(a+b)}{c/(c+d)}$$

Coding

A problem arises in calculating odds ratio and relative risk using some statistical packages because the format of the table that is required to compute the correct statistics is different from the format used in clinical epidemiology textbooks. To use SPSS to compute these risk statistics, the variables need to be coded as shown in Table 8.2.

Table 8.2 Possible coding of variables to compute risk

Code	Alternate code	Condition	Interpretation
1	0	Disease absent	Outcome negative
2	1	Disease present	Outcome positive
1	0	Exposure absent	Risk factor negative
2	1	Exposure present	Risk factor positive

This will invert the table shown in Table 8.1 but as shown later in this chapter, this will allow the odds ratio to be read directly from the SPSS output generated in both the *Frequencies → Crosstabs* and the *Regression → Binary Logistic* menus.

If the reverse notation is used as in Table 8.1, the odds ratio and relative risk statistics printed by SPSS have to be inverted to obtain the correct direction of effect. The options are to either

- code the data as shown in Table 8.2 and in Table 7.3 in Chapter 7, which inverts the location of cells in Table 8.1 but not the statistics or
- code the data as shown in Table 8.1 which inverts the statistics but not the table.

In this chapter, the first option is used so that the layout of the tables is as shown in Table 7.3 in Chapter 7.

Odds ratio vs relative risk

Both odds ratio and relative risk are invaluable statistics for describing the magnitude of the relationship between the exposure and the outcome variables because they provide a size of effect that adds to the information provided by the chi-square value. A chi-square test indicates whether the difference in the proportion of participants with and without disease in the exposure present group and the exposure absent group is statistically significant, but an odds ratio quantifies the relative size of the difference between the groups.

The advantage of calculating the relative risk is that it has an intuitive interpretation. A relative risk of 2.0 indicates that the prevalence of disease in the exposed cases is twice as high as the prevalence in the non-exposed cases. Although a relative risk should not be calculated for some study designs, for example case–control designs, it is a useful statistic to describe risk in studies in which the participants are selected as a random sample of the population.

Odds ratio is a less valuable statistic because it represents the odds of disease, which is not as intuitive as the relative risk. Although the odds ratio is not the easiest of statistics to explain or understand, it is widely used for describing an association between an exposure and a disease because it can be calculated from studies of any design, including cross-sectional, cohort studies, case–control studies and experimental trials as shown in Table 8.3.

Table 8.3 Study type and statistics available

Type of study	Odds ratio	Relative risk
Cross-sectional	Yes	Yes
Cohort	Yes	Sometimes
Case–control	Yes	No
Clinical trial	Yes	Sometimes

Odds ratio has the advantage that it can be used to make direct comparisons of results from studies of different designs and, for this reason, odds ratios are often used in meta-analyses. The odds ratio and the relative risk are always in the same direction of risk or protection. However, the odds ratio does not give a good approximation of the relative risk when the exposure and/or the disease is relatively common[3]. The odds ratio is always larger than relative risk and therefore generally overestimates the true association between variables. For this reason, odds ratios are sometimes referred to as a poor man's relative risk.

The assumptions for using odds ratio and relative risk are exactly the same as the assumptions for using chi-square tests shown in Box 7.2 in Chapter 7.

Odds ratio

The odds ratio is the odds of a person having a disease if exposed to the risk factor divided by the odds of a person having a disease if not exposed to the risk factor. Conversely, an odds ratio can be interpreted as the odds of a person having been exposed to a factor when having the disease compared to the odds of a person not having been exposed to a factor when not having the disease. This converse interpretation is useful for case–control studies in which participants are selected on the basis of their disease status and their exposures are measured. In this type of study, the odds ratio is interpreted as the odds that a case has been exposed to the risk factor of interest compared to the odds that a control has been exposed.

Table 8.4 2 × 2 crosstabulation of disease and exposure

	Disease absent	**Disease present**	**Total**
Exposure absent	75 *d*	60 *c*	135
Exposure present	*b* 25	*a* 40	65
Total	100	100	200

The calculation of the odds ratio from the data shown in Table 8.4 is as follows:

$$\begin{aligned}\text{Odds ratio} &= (a/b)/(c/d)\\ &= (40/25)/(60/75)\\ &= (8/5)/(4/5)\\ &= 2.0\end{aligned}$$

Obviously, if an odds ratio is 1.0 then the odds that people with and without the disease have been exposed is equal and the exposure presents no difference in risk. An odds ratio of 2.0 can be interpreted as the odds that an exposed person has the disease present is twice that of the odds that a non-exposed person has the disease present. An odds ratio calculated in this way from a

2 × 2 table is called an unadjusted odds ratio because it is not adjusted for the effects of possible confounders. Odds ratios calculated using logistic regression are called adjusted odds ratios because they are adjusted for the effects of the other variables in the model.

Another way that an odds ratio of 2 can be interpreted is that if a person who is exposed to a risk factor and a person who is not exposed to the same risk factor are compared, a gambler would break even by betting 2:1 that the person who had been exposed would have the disease[1]. Naturally, these interpretations are not intuitive for most researchers and clinicians.

The size of odds ratio that is important is often debated and in considering this the clinical importance of the outcome and the number of people exposed need to be taken into account. An odds ratio above 2.0 is usually important. However, a smaller odds ratio between 1.0 and 2.0 can have public health importance if a large number of people are exposed to the factor of interest. For example, approximately 25% of the 5 million children aged between 1 and 14 years living in Australasia have a mother who smokes. The odds ratio for children to wheeze if exposed to environmental tobacco smoke is 1.3, which is close to 1.0. Based on this odds ratio and the high exposure rate, a conservative estimate is that 320 000 children wheeze as a result of being exposed, which amounts to an important public health problem[4]. If only 5% of children were exposed or if the outcome was more trivial, the public health impact would be less important.

Research question

The spreadsheet **asthma.sav** contains data from a random cross-sectional sample of 2464 children aged 8 to 10 years in which the exposure of allergy to housedust mites (HDM), the exposure to respiratory infection in early life, the characteristic gender and the presence of the disease, that is, asthma, were measured in all children.

Question: Are HDM allergy, early infection or gender independent risk factors for asthma in this sample of children?

Null hypothesis: That HDM allergy, respiratory infection in early life and gender are not independent risk factors for asthma.

Variables: Outcome variable = Diagnosed asthma (categorical, two levels)

Explanatory variables (risk factors) = allergy to HDM (categorical, two levels), early infection (categorical, two levels) and gender (categorical, two levels).

The SPSS commands shown in Box 8.1 can be used to obtain the crosstabulations for the three risk factors and their risk statistics. In calculating risk, the risk factors are entered in the rows, the outcome in the columns and the row percentages are requested. Each explanatory variable is crosstabulated separately with the outcome variable so three different crosstabulation tables are produced.

Box 8.1 SPSS commands to obtain risk statistics

SPSS Commands

asthma – SPSS Data Editor

Analyze → Descriptive Statistics → Crosstabs

Crosstabs

Highlight Allergy to HDM, Early infection, and Gender and click into Row(s)

Highlight Diagnosed asthma and click into Column(s)

Click Statistics

Crosstabs: Statistics

Tick Chi-square, tick Risk, Click Continue

Crosstabs

Click Cells

Crosstabs: Cell Display

Tick Observed under Counts (default), tick Row under Percentages, click Continue

Crosstabs

Click OK

*Allergy to HDM * Diagnosed asthma*

Crosstab

			Diagnosed asthma		
			No	**Yes**	**Total**
Allergy to HDM	No	Count	1414	125	1539
		% within allergy to HDM	91.9%	8.1%	100.0%
	Yes	Count	529	396	925
		% within allergy to HDM	57.2%	42.8%	100.0%
Total		Count	1943	521	2464
		% within allergy to HDM	78.9%	21.1%	100.0%

Chi-Square Tests

	Value	***df***	**Asymp. sig. (two-sided)**	**Exact sig. (two-sided)**	**Exact sig. (one-sided)**
Pearson chi-square	416.951[b]	1	0.000		
Continuity correction[a]	414.874	1	0.000		
Likelihood ratio	411.844	1	0.000		
Fisher's exact test				0.000	0.000
Linear-by-linear association	416.782	1	0.000		
N of valid cases	2464				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 195.59.

Risk Estimate

		95% confidence interval	
	Value	Lower	Upper
Odds ratio for allergy to HDM (no/yes)	8.468	6.765	10.600
For cohort diagnosed asthma = no	1.607	1.516	1.702
For cohort diagnosed asthma = yes	0.190	0.158	0.228
N of valid cases	2464		

The Crosstab table for HDM allergy shows that in the group of children who did not have HDM allergy 8.1% had been diagnosed with asthma and in the group of children who did have HDM allergy 42.8% had been diagnosed with asthma. The Pearson's chi-square value in the Chi-Square Tests table is used to assess significance because the sample size is in excess of 1000. The P value is highly significant at $P < 0.0001$ indicating that the frequency of HDM allergy is significantly different between the two groups. The odds ratio could be calculated from the crosstabulation as (396/529)/(125/1414), which is 8.468. This is shown in the Risk Estimate table, which also gives the 95% confidence interval. The odds ratio for the association between a diagnosis of asthma and HDM allergy is large at 8.468 (95% CI 6.765 to 10.60) reflecting the large difference in percentages of outcome given exposure and thus a strong relation between the two variables in this sample of children. The 95% confidence interval does not contain the value of 1.0, which represents no difference in risk, and therefore is consistent with an odds ratio that is statistically significant.

The cohort statistics below the odds ratio can also be used to generate relative risk, which is explained later in this chapter.

*Early infection * Diagnosed asthma*

Crosstab

			Diagnosed asthma		
			No	Yes	Total
Early infection	No	Count	1622	399	2021
		% within early infection	80.3%	19.7%	100.0%
	Yes	Count	321	122	443
		% within early infection	72.5%	27.5%	100.0%
Total		Count	1943	521	2464
		% within early infection	78.9%	21.1%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Pearson chi-square	13.247[b]	1	0.000		
Continuity correction[a]	12.784	1	0.000		
Likelihood ratio	12.599	1	0.000		
Fisher's exact test				0.000	0.000
Linear-by-linear association	13.242	1	0.000		
N of valid cases	2464				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 93.67.

Risk Estimate

		95% confidence interval	
	Value	Lower	Upper
Odds ratio for early infection (no/yes)	1.545	1.221	1.955
For cohort diagnosed asthma = no	1.108	1.042	1.178
For cohort diagnosed asthma = yes	0.717	0.602	0.854
N of valid cases	2464		

The second Crosstab table shows that 19.7% of children in the group who did not have an early respiratory infection had a diagnosis of asthma compared with 27.5% of the group who did have an early respiratory infection. Although the difference in percentages in this table (27.5% vs 19.7%) is not as large as for HDM allergy, the Pearson's chi-square value in the Chi-Square Tests table shows that this difference is similarly highly significant at $P < 0.0001$. However, the Risk Estimate table shows that the odds ratio for the association between a diagnosis of asthma and an early respiratory infection is much lower than for HDM allergy at 1.545 (95% CI 1.221 to 1.955). Again, the statistical significance of the odds ratio is reflected in the 95% confidence interval, which does not contain the value of 1.0, which represents no difference in risk.

*Gender * Diagnosed asthma*

Crosstab

			Diagnosed asthma		
			No	Yes	Total
Gender	Female	Count	965	223	1188
		% within gender	81.2%	18.8%	100.0%
	Male	Count	978	298	1276
		% within gender	76.6%	23.4%	100.0%
Total		Count	1943	521	2464
		% within gender	78.9%	21.1%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Pearson chi-square	7.751[b]	1	0.005		
Continuity correction[a]	7.478	1	0.006		
Likelihood ratio	7.778	1	0.005		
Fisher's exact test				0.006	0.003
Linear-by-linear association	7.747	1	0.005		
N of valid cases	2464				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 251.20.

Risk Estimate

		95% confidence interval	
	Value	Lower	Upper
Odds ratio for gender (female/male)	1.319	1.085	1.602
For cohort diagnosed asthma = no	1.060	1.017	1.104
For cohort diagnosed asthma = yes	0.804	0.689	0.938
N of valid cases	2464		

For gender, the Crosstab table shows that 18.8% of females had a diagnosis of asthma compared with 23.4% of males. At $P = 0.005$, the Pearson's chi-square value in the Chi-Square Tests table is less significant than for the other two variables and the odds ratio of 1.319 (95% CI 1.085 to 1.602) in the Risk Estimate table is also smaller, reflecting the smaller difference in proportions in diagnosed asthma between the two gender groups.

Reporting the results

The results from these tables can be presented as shown in Table 8.5. When reporting an odds ratio or relative risk, the per cent of cases with the outcome in the two comparison groups of interest are included. It is often useful to rank variables in order of the magnitude of risk.

Table 8.5 Unadjusted associations between risk factors and diagnosed asthma in a random sample of 2464 children aged 8 to 10 years

Risk factor (exposure)	%diagnosed asthma in exposed group	% diagnosed asthma in non-exposed group	Unadjusted odds ratio and 95% CI	Chi-square	*P* value
Allergy to HDM	42.8%	8.1%	8.5 (6.8, 10.6)	417.0	<0.0001
Early infection	27.5%	19.7%	1.5 (1.2, 2.0)	13.2	<0.0001
Gender	23.4%	18.8%	1.3 (1.1, 1.6)	7.8	0.005

Odds ratios larger than 1.0 are reported with only one decimal place because the precision of 1/100th or 1/1000th of an estimate of risk is not required. The decision of whether to include a column with the chi-square values is optional since the only interpretation of the chi-square value is the *P* value. From the table, it is easy to see how the odds ratio describes the strength of the associations between variables in a way that is not discriminated by the *P* values.

Protective odds ratios

An odds ratio greater than 1.0 indicates that the risk of disease in the exposed group is greater than the risk in the non-exposed group. If the odds ratio is less than 1.0, then the risk of disease in the exposed group is less than the risk in the non-exposed group.

Whether odds ratios represent risk or protection largely depends on the way in which the data are coded. For example, having HDM allergy is a strong risk factor for diagnosed asthma in the study sample but if the coding had been reversed with not having HDM allergy coded as 2, then not having HDM allergy would be a strong protective factor. For ease of interpretation, comparison and communication, it is usually better to present all odds ratios in the direction of risk rather than presenting some as risk and some as protection.

To illustrate this, the commands shown in Box 1.10 can be used to reverse the coding of HDM allergy from 2 = exposure to 1 = exposure and from 1 = no exposure to 2 = no exposure. In this example, the new variable is called hdm2 and its values have been added in Variable View before conducting any analyses. The SPSS commands shown in Box 8.1 can then be used with allergy to HDM re-coded as the row variable, diagnosed asthma as the column variable and the row percentages requested.

Allergy to HDM – Re-coded * Diagnosed Asthma Crosstabulation

			Diagnosed asthma		
			No	**Yes**	**Total**
Allergy to HDM – re-coded	Allergy	Count	529	396	925
		% within allergy to HDM – re-coded	57.2%	42.8%	100.0%
	No Allergy	Count	1414	125	1539
		% within allergy to HDM – re-coded	91.9%	8.1%	100.0%
Total		Count	1943	521	2464
		% within allergy to HDM – re-coded	78.9%	21.1%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Pearson chi-square	416.951[b]	1	0.000		
Continuity correction[a]	414.874	1	0.000		
Likelihood ratio	411.844	1	0.000		
Fisher's exact test				0.000	0.000
Linear-by-linear association	416.782	1	0.000		
N of valid cases	2464				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 195.59.

Risk Estimate

		95% confidence interval	
	Value	Lower	Upper
Odds ratio for allergy to HDM – recoded (allergy/no allergy)	0.118	0.094	0.148
For cohort diagnosed asthma = no	0.622	0.588	0.659
For cohort diagnosed asthma = yes	5.271	4.386	6.334
N of valid cases	2464		

The per cent of children with diagnosed asthma in the exposed and unexposed groups and the *P* value are obviously exactly the same as before. The only difference in the Crosstabulation table is that the rows have been interchanged. The odds ratio is now a protective factor of 0.118 (95% 0.094 to 0.148) rather than a risk factor of 8.468 (95% CI 6.765 to 10.60) as it was in the first analysis.

Summary statistics of odds ratio can easily be changed from protection to risk or vice versa by calculating the reciprocal value, that is

$$\begin{aligned}\text{odds ratio (risk)} &= 1/\text{odds ratio (protection)}\\ &= 1/0.118\\ &= 8.474\end{aligned}$$

When recalculated, the upper confidence interval becomes the lower confidence interval and vice versa.

Figure 8.1 shows an odds ratio expressed as a risk factor or as a protective factor. The *x*-axis is a logarithmic scale because odds ratios are derived from logarithmic values. In Figure 8.1, the dotted line passing through 1 indicates the line of no effect, that is, no difference in risk. When a factor is coded as risk or protection, the effect size is the same because on a logarithmic scale the odds ratios are symmetrical on either side of the line of unity.

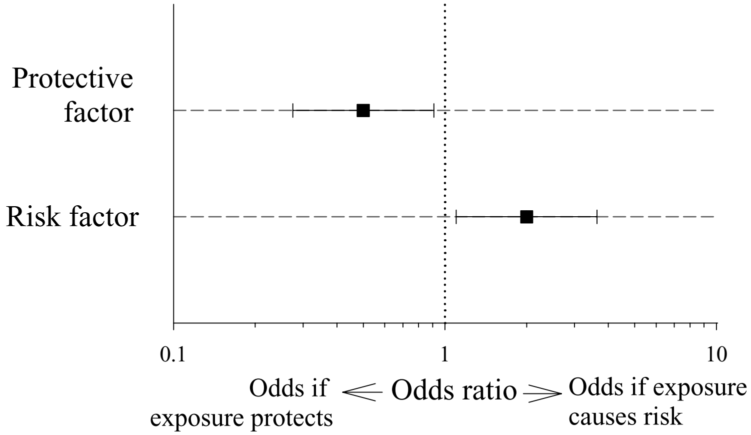

Figure 8.1 Effect of an exposure on a disease shown as both a protective factor and as a risk factor.

Adjusting for inter-relationships between risk factors

A problem with odds ratios calculated from 2 × 2 crosstabulations is that some explanatory factors may be related to one another. If cases with one factor present also tend to have another factor present, the effects of both factors in increasing the odds of disease will be included in each odds ratio. Thus, each odds ratio will be artificially inflated with the effect of the associated exposure, that is confounding will be present. Logistic regression is used to calculate the effects of risk factors as independent odds ratios with the effects of other confounders removed. These odds ratios are called adjusted odds ratios.

Figure 8.2 shows the percentage of cases with disease in each of three exposure groups. In group 1, participants had no exposure, in group 2 participants had exposure to factor I and in group 3 participants had exposure to factor I and factor II. If an unadjusted odds ratio were used to calculate the risk of disease in the presence of exposure to factor I, then in a bivariate analysis, groups 2 and 3 would be combined and compared with group 1. The effect of including cases also exposed to factor II would inflate the estimate of risk because their rate of disease is higher than for cases exposed to factor 1. Logistic regression is used to mathematically separate out the independent risk associated with exposure to factor I or to factor II.

Binary logistic regression

Binary logistic regression is not really a regression analysis in the classic sense of the term but is a mathematical method to measure the effects of binary risk factors on a binary outcome variable whilst adjusting for inter-relationships between them. In binary logistic regression, the variables that

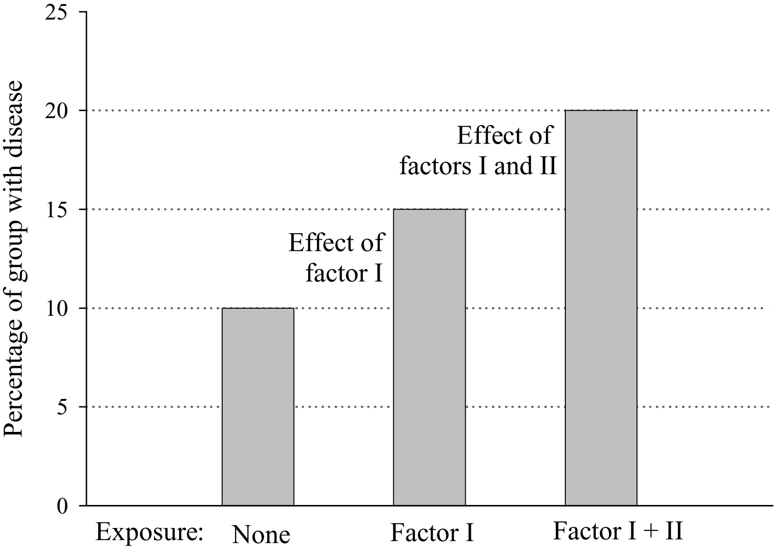

Figure 8.2 Rate of disease in group not exposed and in groups exposed to factor I or to both factors I and II.

affect the probability of the outcome are measured as odds ratios which are called adjusted odds ratios.

Logistic regression is primarily used to determine which binary explanatory variables independently predict the outcome, when the outcome is a binary variable[5]. The outcome variable normally reflects the presence or absence of a condition or a disease, for example, the presence or absence of asthma, or the occurrence or absence of a heart attack.

The assumptions for using logistic regression are shown in Box 8.2. In addition, the assumptions for the chi-square test as shown in Box 7.2 must also be met.

Box 8.2 Assumptions for using logistic regression

The assumptions that must be met when using logistic regression are as follows:

- the sample is representative of the population to which inference will be made
- the sample size is sufficient to support the model
- the data have been collected in a period when the relationship between the outcome and the explanatory variable/s remains constant
- all important explanatory variables are included
- the explanatory variables do not have a high degree of collinearity with one another

- if an ordered categorical variable or a continuous variable is included as an explanatory variable, the effect over levels of the factor must be linear
- alternate outcome and intervening variables are not included as explanatory variables

Although the explanatory variables or predictors in the model can be continuous or categorical variables, logistic regression is best suited to measure the effects of exposures or explanatory variables that are binary variables. Continuous variables can be included but logistic regression will produce an estimate of risk for each unit of measurement. Thus, the assumption that the risk effect is linear over each unit of the variable must be met and the relationship should not be curved or have a threshold value over which the effect occurs. In addition, interactions between explanatory variables can be included but these cause the same problems of collinearity as discussed for multiple regression in Chapter 6. Logistic regression is not suitable for matched or paired data or for repeated measures because the measurements are not independent – in these situations, conditional logistic regression is used. In addition, variables that are alternative outcome variables because they are on the same pathway of development as the outcome variable must not be included as independent risk factors.

A large sample size is usually required to support a reliable binary logistic regression model because a cell is generated for each unit of the variable. The data are divided into a multi-dimension array of cells in exactly the same way as for fuctorial ANOVA shown in Table 5.6 in Chapter 5 but the outcome variable is also included in the array. If three variables each with two levels are included in the analysis, for example an outcome and two explanatory variables, the number of cells in the model will be 2 × 2 × 2, or eight cells. As with chi-square analyses, a general rule of thumb is that the number of cases in any one cell should be at least 10. When there are empty cells or cells with a small number of cases, estimates of risk can become unstable and unreliable. Thus, it is important to have an adequate sample size to support the analysis.

Although SPSS provides automatic forward and backward stepwise processes for building multivariate models, it is better to build a logistic regression model using the same sequential method described for multiple regression in Chapter 6. Using this method, variables are added to the model one at a time in order of the magnitude of the chi-square association, starting with the largest estimate. At each step, changes to the model can be examined to assess collinearity and instability in the model.

If an *a priori* decision is made to include known confounders, these can be entered first into the logistic regression and the model built up from there. Alternatively, confounders can be entered at the end of the model building sequence and only retained in the model if they change the size of the coefficients of the variables already in the model by more than 10%. It is important to decide which is the most appropriate method of entering the variables before the analysis is conducted.

At each step of adding a variable to the model, it is important to compare the *P* values, the standard errors and the odds ratios in the model from Block 1 of 1 with the values from the second model in Block 2 of 2. A standard error that increases by an important amount, say 10%, is an indication that the model has become less precise. In this situation, the model is less stable as a result of two or more variables having some degree of collinearity and thus sharing variation. The effect of shared variation is to inflate the standard errors. If this occurs, then one of the variables must be removed. If the standard error decreases, the model has become more precise. This indicates that the variable added to the model is a good predictor of the outcome and explains some of the variance. As with any multivariate model, the decision of which variable to remove or maintain is based on biological plausibility for the effect and decisions about the variables that can be measured with most accuracy.

Research question

The risk factors for asthma in the research question can now be examined in a multivariate model by building a logistic regression using the SPSS commands shown in Box 8.3. Based on the magnitude of the chi square values, the variable allergy to HDM will be entered first, then early infection and finally gender.

Box 8.3 SPSS commands to build a logistic regression model

SPSS Commands

asthma – SPSS Data Editor
Analyze → Regression → Binary Logistic
Logistic Regression
Highlight Diagnosed asthma and click into Dependent
Highlight Allergy to HDM and click into Covariates
Method = Enter (default)
Under Block 1 of 1, click Next
Highlight Early infection and click into Covariates under Block 2 of 2
Method = Enter (default)
Click OK

Logistic regression

Model Summary

Step	−2 Log likelihood	Cox & Snell *R* square	Nagelkerke *R* square
1	2130.337	0.154	0.239

Variables in the Equation

		B	S.E.	Wald	*df*	Sig.	Exp(*B*)
Step	HDM	2.136	0.115	347.771	1	0.000	8.468
1[a]	Constant	−4.562	0.198	530.349	1	0.000	0.010

[a] Variable(s) entered on step 1: HDM.

In the Model Summary table, the Cox and Snell *R* square is similar to the multiple correlation coefficient in linear regression and measures the strength of the association. This coefficient which takes sample size into consideration is based on log likelihoods and cannot reach its maximum value of 1.[4] The Nagelkerke *R* square is a modification of the Cox and Snell so that a value of 1 can be obtained[6]. Consequently, the Nagelkerke *R* square is generally higher than Cox's and has values that range between 0 and 1. In this model, the Nagelkerke *R* square indicates that 23.9% of the variation in diagnosed asthma is explained by HDM allergy.

The Variables in the Equation table shows the model coefficients. The *B* estimate for HDM allergy of 2.136 is the odds ratio in units of natural logarithms, that is to the base e. The standard error of this estimate in log units is 0.115. When adding further variables to the model, it is important that this standard error does not inflate by more than 10%. The actual odds ratio of 8.468 is shown as the anti-log (or exponential) of the *B* estimate in the column exp(*B*).

The Wald statistic in the Variables in the Equation table has a chi-square distribution and is the result of dividing the *B* value by its standard error and then squaring the result. This value is used to calculate the significance (*P*) value for each factor in the model. In logistic regression, the constant is used in the prediction of probabilities but does not have a practical interpretation.

Block 2: Method = Enter

Model Summary

Step	−2 Log likelihood	Cox & Snell *R* square	Nagelkerke *R* square
1	2125.062	0.156	0.242

Variables in the Equation

		B	S.E.	Wald	*df*	Sig.	Exp(*B*)
Step	HDM	2.123	0.115	342.608	1	0.000	8.360
1[a]	INFECT	0.307	0.133	5.369	1	0.020	1.360
	Constant	−4.911	0.252	380.375	1	0.000	0.007

[a] Variable(s) entered on step 1: INFECT.

The Model Summary table from Block 2 shows that the Nagelkerke *R* square has increased slightly from 0.239 to 0.242 and the odds ratio for HDM allergy has decreased slightly from 8.467 to 8.360. Importantly, the standard error for HDM allergy has remained unchanged at 0.115 indicating that the model is stable. The odds ratio for infection, which is the exponential of the beta coefficient (*B*) 0.307, that is 1.36, is significant at $P = 0.02$. This estimate of risk is reduced compared to the unadjusted odds ratio obtained from the 2 × 2 table.

The effect of gender can be added to the model using the commands shown in Box 8.3 by entering the variables allergy to HDM and early infection for the stable model in Block 1 of 1 and entering gender in Block 2 of 2.

Logistic regression

Model Summary

Step	−2 Log likelihood	Cox & Snell *R* square	Nagelkerke *R* square
1	2124.788	0.156	0.242

Variables in the Equation

		B	S.E.	Wald	*df*	Sig.	Exp(*B*)
Step 1[a]	HDM	2.118	0.115	338.103	1	0.000	8.313
	INFECT	0.302	0.133	5.155	1	0.023	1.353
	GENDER	0.058	0.110	0.274	1	0.600	1.059
	Constant	−4.985	0.289	297.409	1	0.000	0.007

[a] Variable(s) entered on step 1: GENDER.

The addition of gender does not change the *R* square statistics in the Model Summary table and hardly changes the odds ratio for HDM allergy in the Variables in the Equation table. The odds ratio for HDM allergy falls slightly from 8.360 to 8.313 and there is no change in the standard error of 0.115. The odds ratio for infection falls slightly from 1.360 to 1.353, again with no change in the standard error of 0.133. However, gender which was a significant risk factor in the unadjusted analysis at $P = 0.005$ is no longer significant in the model with $P = 0.60$. The unadjusted odds ratio for gender was 1.319 in bivariate analyses compared to the adjusted value which is now 1.059.

The reduction in this odds ratio suggests that there is a degree of confounding between gender and HDM allergy or infection. The extent of the confounding can be investigated using the SPSS commands in Box 7.3 with allergy to HDM and early infection entered in the rows, gender entered in the columns and column percentages requested.

*Allergy to HDM * Gender*

Crosstab

			Gender		
			Female	Male	Total
Allergy to HDM	No	Count	805	734	1539
		% within gender	67.8%	57.5%	62.5%
	Yes	Count	383	542	925
		% within gender	32.2%	42.5%	37.5%
Total		Count	1188	1276	2464
		% within gender	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Pearson chi-square	27.499[b]	1	0.000		
Continuity correction[a]	27.064	1	0.000		
Likelihood ratio	27.600	1	0.000		
Fisher's exact test				0.000	0.000
Linear-by-linear association	27.487	1	0.000		
N of valid cases	2464				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 445.98.

*Early infection * Gender*

Crosstab

			Gender		
			Female	Male	Total
Early infection	No	Count	1016	1005	2021
		% within gender	85.5%	78.8%	82.0%
	Yes	Count	172	271	443
		% within gender	14.5%	21.2%	18.0%
Total		Count	1188	1276	2464
		% within gender	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	*df*	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Pearson chi-square	19.065[b]	1	0.000		
Continuity correction[a]	18.610	1	0.000		

Continued

	Value	*df*	Asymp. sig. (two-sided)	Exact sig. (two-sided)	Exact sig. (one-sided)
Likelihood ratio	19.228	1	0.000		
Fisher's exact test				0.000	0.000
Linear-by-linear association	19.058	1	0.000		
N of valid cases	2464				

[a] Computed only for a 2 × 2 table.

[b] 0 cell (0.0%) has expected count less than 5. The minimum expected count is 213.59.

The tables show that allergy to housedust mites and early respiratory infection are both related to gender, with males having a higher percentage of allergy and early respiratory infections. Thus, gender was a risk factor in the unadjusted estimates because of confounding between gender and the other two risk factors. The logistic regression shows that once the effects of confounding are removed, gender is no longer a significant independent risk factor for diagnosed asthma.

The interpretation of this model is that boys have a higher rate of diagnosed asthma because they have a higher rate of allergy to HDM and a higher rate of early respiratory infection than girls, and not because they are male per se. Separating out the confounding and identifying the independent effects of risk factors makes an invaluable contribution towards identifying pathways to disease.

Computing confidence intervals from logistic regression output

Odds ratios should be reported with their 95% confidence intervals although the intervals are not provided in the SPSS output. The calculation is simple but it needs to take account of the fact that the odds ratio (B) and the SE are in units of natural logarithms. Few people can think in logarithmic units. Thus, once the 95% confidence intervals are calculated, the anti-log of the units needs to be obtained for presenting summary statistics in a way that increases the transparency of the results and simplifies communicating the findings.

The 95% CI can be calculated in logarithmic units as follows:

$$95\%\ \text{CI} = \text{Beta} \pm (1.96 \times \text{SE})$$

and then the antilog of the two values can be calculated. This can be undertaken in an Excel spreadsheet as shown in Table 8.6. The beta coefficients and the standard errors (SE) are taken directly from the SPSS output. The formulae that are used to calculate the 95% confidence intervals around the odds ratios derived from SPSS are shown below, where exp indicates an exponential conversion. In Excel, clicking on Insert and then Function, the exponential function is listed as EXP under the Math and Trig Function Category.

$$\begin{aligned}
\text{Odds ratio} &= \exp\ (\text{beta}) \\
\text{Lower CI} &= \exp\ (\text{beta} - 1.96 \times \text{SE}) \\
\text{Upper CI} &= \exp\ (\text{beta} + 1.96 \times \text{SE}) \\
\text{Width down} &= \text{odds ratio} - \text{lower CI} \\
\text{Width up} &= \text{upper CI} - \text{odds ratio}
\end{aligned}$$

Table 8.6 Excel spreadsheet to compute confidence intervals around odds ratios derived from logistic regression

	Beta	SE	1.96 × SE	Odds ratio	Lower	Upper	Width down	Width up
HDM	2.118	0.115	0.225	8.313	6.637	10.417	1.678	2.102
Infection	0.302	0.133	0.261	1.353	1.042	1.755	0.310	0.403
Gender	0.058	0.11	0.216	1.059	0.854	1.315	0.206	0.255

Reporting the results

When reporting odds ratios from any type of study design, the percentages from which they are derived must also be reported so that the level of exposure can be used to interpret the findings. In this research question, the data were derived from a cross-sectional study and thus it is important to report the proportion of children who had asthma in the groups that were exposed or not exposed to the risk factors of interest as shown in Table 8.7. In a case–control study, it would be important to report the per cent of participants in the case and control groups who were exposed to the factors of interest. It is also important to report the unadjusted and adjusted values so that the importance of confounding factors is clear. The adjusted odds ratios from the binary logistic regression are smaller but provide an estimate that is not biased by confounding.

Table 8.7 Unadjusted and adjusted risk factors for children to have asthma

Risk factor	Exposed % with asthma	Non-exposed % with asthma	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)	*P* value
HDM allergy	42.8%	8.1%	8.5 (6.8, 10.6)	8.3 (6.6, 10.4)	<0.0001
Early infection	27.5%	19.7%	1.5 (1.2, 2.0)	1.4 (1.0, 1.8)	0.023
Gender	23.4%	18.8%	1.4 (1.1, 1.6)	1.1 (0.9, 1.3)	0.600

Odds ratios are multiplicative. Table 8.7 shows that the odds ratio for the association between childhood asthma and allergy to HDM is 8.3. However, the odds ratio for children to have diagnosed asthma is they are exposed to both allergy to HDM and to an early respiratory infection compared to the odds they are not exposed to either risk factor is 8.3 × 1.4, or 11.6.

Plotting the results in a figure

The lower and upper 95% confidence intervals have different widths as a result of being computed in logarithmic units, therefore they need to be overlaid as separate plots when using SigmaPlot as shown in Box 8.4. The estimates of odds ratios and confidence interval widths obtained in Excel can be entered into SigmaPlot worksheet with the odds ratio in column 1, the width down in column 2 and the width up in column 3 as follows:

Column 1	Column 2	Column 3
8.314	1.678	2.102
1.353	0.310	0.403
1.060	0.206	0.255

The graph can then be plotted using the commands shown in Box 8.4.

Box 8.4 SigmaPlot commands to plot odds ratios

SigmaPlot Commands

```
SigmaPlot – [Data 1*]
          Graph → Create Graph
Create Graph - Type
          Highlight Scatter Plot, click Next
Create Graph - Style
          Highlight Horizontal Error Bars, click Next
Create Graph – Error Bars
          Symbol Values = Worksheet Columns (default), click Next
Create Graph – Data Format
          Data Format = Highlight Many X, click Next
Create Graph – Select Data
          Data for Bar = use drop box and select Column 1
          Data for Error = use drop box and select Column 2
          Click Finish
```

The sequence is then repeated in *Graph → Add Plot* with column 1 again as the data for the bar and column 3 as the data for the error. Once this basic graph is obtained, the labels, symbols, axes, ticks and labels can be customised under the *Graph → Options* menus to obtain Figure 8.3. The x-axis needs to be a logarithmic base 10 scale, the first plot should have negative error bars only and the second plot should have positive error bars only.

Figure 8.3 shows the relative importance of the odds ratios. Early infection and allergy to HDM are significant risk factors which is reflected by their 95%

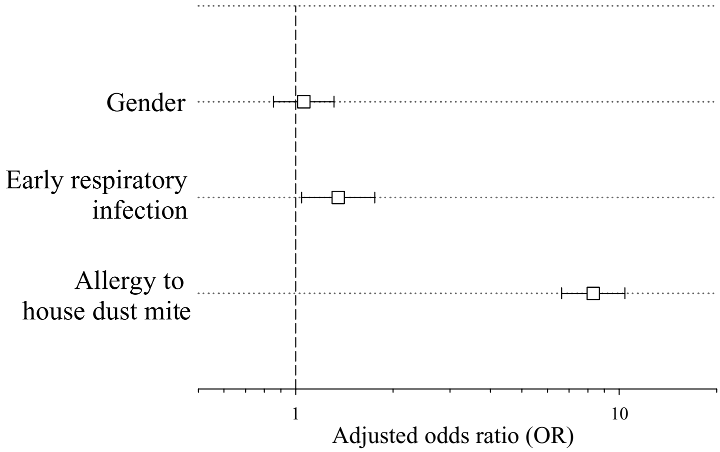

Figure 8.3 Independent risk factors for diagnosed asthma in children.

confidence intervals not crossing the line of no effect (unity). For gender, the odds ratio is close to unity and the confidence intervals lie on either side of the line of unity indicating an effect from protection to risk, which is therefore ambiguous.

Relative risk

Relative risk can only be used when the sample is randomly selected from the population and cannot be used in other studies, such as case–control studies or some clinical trials, in which the percentage of the sample with the disease is determined by the sampling method.

If the summary data shown in Table 8.4 had been collected from a random sample the relative risk would be calculated as follows:

$$\begin{aligned}\text{Relative risk} &= a/(a+c)/b/(b+d)\\ &= (40/100)/(25/100)\\ &= 1.6\end{aligned}$$

Thus the risk estimates are calculated by dividing the per cent of disease positive cases in one row by the per cent of disease positive cases in the other row. The calculation shows how the odds ratio of 2.0 calculated previously with the same data can overestimate the relative risk of 1.6.

In requesting risk statistics in conjunction with a 2 × 2 table in SPSS, three estimates are shown in the Risk Estimate table. The first set of statistics is the odds ratio and the next two sets of estimates are labelled ‘For cohort = No’ and ‘For cohort = Yes’. If the 2 × 2 table is set up appropriately, one of these two statistics is the relative risk. If the 2 × 2 table is not set up appropriately, relative risk has to be computed from the risk estimates.

For obtaining relative risk in SPSS, the crosstabulation table needs to be set up with the outcome in the columns, the risk factor in the rows and the row percentages requested. If a table is constructed in this way, then either of the following two options can be used.

Option 1

The risk factor but not the outcome has to be re-coded with the exposure present (yes) coded as 1 and the exposure absent (no) coded as 2.

On the spreadsheet **asthma.sav**, allergy to HDM has been re-coded in this way into the variable HDM2. This coding is exactly opposite to the coding needed to easily interpret the output from logistic and linear regressions. This coding scheme will 'invert' the crosstabulation table so that the positive exposure is shown on the top row and no exposure is shown on the row below. This table with HDM allergy re-coded, which was shown previously, is shown again below. The relative risk can then be calculated as the row percentage for positive outcome divided by the row percentage for negative outcome, that is 42.8/8.1 or 5.28. This statistic is given in the line 'For cohort = Yes', with a negligible difference from the calculated value resulting from rounding of decimal places.

Crosstabs

Allergy to HDM – Re-coded * Diagnosed Asthma Crosstabulation

			Diagnosed asthma		
			No	Yes	Total
Allergy to HDM – recoded	Allergy	Count	529	396	925
		% within allergy to HDM – recoded	57.2%	42.8%	100.0%
	No allergy	Count	1414	125	1539
		% within allergy to HDM – recoded	91.9%	8.1%	100.0%
Total		Count	1943	521	2464
		% within allergy to HDM – recoded	78.9%	21.1%	100.0%

Risk Estimate

		95% confidence interval	
	Value	Lower	Upper
Odds ratio for HDM allergy – recoded (allergy/no allergy)	0.118	0.094	0.148
For cohort diagnosed asthma = no	0.622	0.588	0.659
For cohort diagnosed asthma = yes	5.271	4.386	6.334
N of valid cases	2464		

In the Risk Estimate table, 'For cohort diagnosed asthma = yes' shows the relative risk for children to have diagnosed asthma in the presence of HDM allergy is 5.271 (95% CI 4.386, 6.334). As with odds ratio, only the number of decimal places that infer a precision that can be interpreted is reported so the risk estimates from this table would be reported as a relative risk of 5.3 (95% CI 4.4, 6.3).

Option 2

If the risk factor for exposure is maintained as coded as 1 for exposure absent (no) and 2 for exposure present (yes), then the table that was obtained previously is shown again below.

Allergy to HDM * Diagnosed Asthma Crosstabulation

			Diagnosed asthma		
			No	**Yes**	**Total**
Allergy to HDM	No	Count	1414	125	1539
		% within allergy to HDM	91.9%	8.1%	100.0%
	Yes	Count	529	396	925
		% within allergy to HDM	57.2%	42.8%	100.0%
Total		Count	1943	521	2464
		% within allergy to HDM	78.9%	21.1%	100.0%

Risk Estimate

		95% confidence interval	
	Value	**Lower**	**Upper**
Odds ratio for allergy to HDM (no/yes)	8.468	6.765	10.600
For cohort diagnosed asthma = no	1.607	1.516	1.702
For cohort diagnosed asthma = yes	0.190	0.158	0.228
N of valid cases	2464		

In this case, the relative risk shown in the table is calculated as 8.1/42.8, or 0.190 and is in the direction of protection. The estimate in the direction of risk and the 95% confidence interval can be computed as the reciprocal of the estimates given for 'For cohort diagnosed asthma = yes' as follows:

$1/0.190 = 5.263$
$1/0.158 = 6.329$
$1/0.228 = 4.386$

Thus, the relative risk for children to have asthma in the presence of HDM allergy is 5.3 (95% CI 4.4, 6.3), which is identical to using the first option.

For both options, the estimate 'For cohort ... = no' is the relative risk of children having diagnosed asthma in the group that is not exposed to the risk factor of interest. This statistic is rarely used.

Number needed to be exposed for one additional person to be harmed

In epidemiological studies in which the influence of an exposure is described by an odds ratio, inclusion of the statistic number needed to be exposed for one additional person to be harmed (NNEH) can be a useful statistic that applies to a person rather than to a sample. As such, this statistic provides the number of people who need to be exposed to the risk factor of interest to cause harm to one additional person.

As with calculating NNT in Chapter 7, NNEH is calculated from a 2 × 2 table in which both the outcome and the exposure are coded as binary variables. The statistic NNEH can be easily calculated from a 2 × 2 crosstabulation in which the outcome is entered in the rows, the exposure is entered in the columns and the column percentages are requested. The statistic NNEH is then calculated from the absolute risk increase (ARI), which is simply the difference in the proportion of participants with the outcome of interest in the exposed and unexposed groups. From the tables for asthma and HDM allergy:

$$\begin{aligned}\text{ARI} &= 0.43 - 0.08 = 0.35\\ \text{NNEH} &= 1/\ \text{ARI} = 1/0.35 = 2.9\end{aligned}$$

This indicates that for every three children with allergy to housedust mites, one additional child will be diagnosed with asthma. NNEH is only reported to whole numbers.

For early infection

$$\begin{aligned}\text{ARI} &= 0.275 - 0.197 = 0.078\\ \text{NNEH} &= 1/\text{ARR} = 1/0.078 = 12.8\end{aligned}$$

This indicates that for every 13 children who have respiratory infection in early life, one additional child will be diagnosed with asthma. Obviously, the larger the odds ratio, the fewer the number of people who need to be exposed to cause harm.

Notes for critical appraisal

When critically appraising an article that reports risk statistics, it is important to ask the questions shown in Box 8.5.

Box 8.5 Questions to ask when critically appraising the literature in which risk statistics are presented

The following questions should be asked of studies that report risk statistics:

- If relative risk is reported, was the sample randomly selected?
- Have the proportions of disease in the exposed and non-exposed groups been reported in addition to the odds ratio or relative risk?
- Is it difficult to compare estimates if some of the factors are presented as risk factors and others as protective factors?
- Are confidence intervals presented for all estimates of odds ratio or relative risk?
- Can all of the variables in the model be classified as independent exposure factors or have alternative outcomes and intervening variables also been included?
- What type of method was used to build the logistic regression model and was collinearity between variables tested?

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CHAPTER 9

Categorical and continuous variables: tests of agreement

Truth cannot be defined or tested by agreement with 'the world'; for not only do truths differ for different worlds but the nature of agreement between a world apart from it is notoriously nebulous.

NELSON GOODMAN, PHILOSOPHER

Objectives

The objectives of the chapter are to explain how to:

- measure repeatability of categorical information collected by questionnaires
- measure the repeatability of continuous measurements
- critically appraise the literature that reports tests of agreement

Repeatability

Questionnaires are often tested for repeatability, which is an aspect of measuring agreement. Repeatability is an important issue especially when new instruments are being developed. In any type of research study, measurements that are accurate (repeatable) provide more reliable information. However, studies of repeatability must be conducted in a setting in which they do not produce a false impression of the accuracy of the measurement. Box 9.1 shows the

Box 9.1 Assumptions for measuring repeatability

The following methods must be used when measuring repeatability:

- the method of administration must be identical on each occasion
- at the second administration, both the participant and the rater (observer) must have no knowledge of the results of the first measurement
- the time to the second administration should be short enough so that the condition has not changed since the first administration
- if a questionnaire is being tested, the time between administrations must be long enough for participants to have forgotten their previous responses
- the setting in which repeatability is established must be the same as the setting in which the questionnaire or measurement will be used

assumptions under which the repeatability of categorical measurements and continuous measurements are tested. All of the assumptions relate to study design.

If a questionnaire is to be used in a community setting, then repeatability has to be established in a similar community setting and not for example in a clinic setting where the patients form a well-defined sub-sample of a population. Patients who frequently answer questions about their illness may have well rehearsed responses to questions and may provide an artificial estimate of repeatability when compared to people in the general population who rarely consider aspects of an illness that they do not have.

Repeatability of categorical data

Questionnaires are widely used in research studies to obtain information of personnel characteristics, illnesses and exposure to environmental factors. For a questionnaire to be a useful research tool, the responses must be repeatable, that is they must not have a substantial amount of measurement error. To test repeatability, the questionnaire is administered to the same people on two separate occasions. An important concept is that the condition that the questionnaire is designed to measure must not have changed in the period between administrations and the time period must be long enough for the participants to have little recollection of their previous responses. Repeatability is then measured as the proportion of responses in agreement on the two occasions using the statistic kappa.

Kappa is used to test the agreement between observers or between administrations for both binary and nominal scales. For data with three or more possible responses or for ordered categorical data, weighted kappa should be used. Kappa is an estimate of the proportion in agreement between two administrations or two observers in excess of the agreement that would occur by chance. A value of 1 indicates perfect agreement and a value of 0 indicates no agreement. In general, values less than 0.40 indicate poor agreement, values between 0.41 and 0.60 indicate moderate agreement, values between 0.61 and 0.80 indicate good agreement and above 0.81 indicate very good agreement[1].

Research question

The file **questionnaires. sav** contains the data of three questions which required a yes or no response. The questions were administered on two occasions to the same 50 people at an interval of 3 weeks. The research aim was to measure the repeatability of the questions. It is often important to establish how repeatable questions are because questions that are prone to a significant amount of random error or bias do not make good outcome or explanatory variables. The SPSS commands shown in Box 9.2 can be used to obtain repeatability statistics.

This command sequence can then be repeated to obtain the following tables and statistics for questions 2 and 3 of the questionnaire.

Box 9.2 SPSS commands to measure repeatability

SPSS Commands

questionnaires – SPSS Data Editor

Analyze → Descriptive Statistics → Crosstabs

Crosstabs

Highlight Question 1-time 1 and click into Row(s)

Highlight Question1-time 2 and click into Column(s)

Click on Statistics

Crosstabs: Statistics

Tick Kappa, tick Continue

Crosstabs

Click on Cells

Crosstabs: Cell Display

Tick Observed under Counts (default), tick Total under Percentages

Click Continue

Crosstabs

Click OK

Crosstabs

Question 1 - Time 1 * Question 1 - Time 2 Crosstabulation

			Question 1 - time 2		
			No	**Yes**	**Total**
Question 1- time 1	No	Count	20	15	35
		% of total	40.0%	30.0%	70.0%
	Yes	Count	4	11	15
		% of total	8.0%	22.0%	30.0%
Total		Count	24	26	50
		% of total	48.0%	52.0%	100.0%

Symmetric Measures

	Value	**Asymp. std. error**[a]	**Approx. T**[b]	**Approx. sig.**
Measure of agreement Kappa	0.252	0.123	1.977	0.048
N of valid cases	50			

[a] Not assuming the null hypothesis.

[b] Using the asymptotic standard error assuming the null hypothesis.

From the Crosstabulation, the proportion in agreement is estimated from the per cent in the concordant No at Time 1-No at Time 2 and Yes at Time 1-Yes at Time 2 cells. Thus the proportion in agreement is 40% + 22%, or 0.62 as a proportion. The Symmetric Measures table shows that the kappa value is low at 0.252 indicating poor repeatability after agreement by chance is taken into account. Kappa is always lower than the proportion in agreement.

Although a *P* value is included in the Symmetric Measures table, it is not a good indication of agreement because its interpretation is that the kappa value is significantly different from zero. Measurements taken from the same people on two occasions in order to assess repeatability are highly related by nature and thus the *P* value is expected to indicate some degree of agreement. The standard error is also reported and can be used to calculate a confidence interval around kappa but this is also of little interest.

Crosstabs

Question 2 - Time 1* Question 2 - Time 2 Crosstabulation

			Question 2 - time 2		
			No	**Yes**	**Total**
Question 2 -time 1	No	Count	34	5	39
		% of total	68.0%	10.0%	78.0%
	Yes	Count	6	5	11
		% of total	12.0%	10.0%	22.0%
Total		Count	40	10	50
		% of total	80.0%	20.0%	100.0%

Symmetric Measures

	Value	**Asymp. std. error[a]**	**Approx. T[b]**	**Approx. sig.**
Measure of agreement Kappa	0.337	0.159	2.390	0.017
N of valid cases	50			

[a] Not assuming the null hypothesis.

[b] Using the asymptotic standard error assuming the null hypothesis.

Crosstabs

Question 3 - Time 1 * Question 3 - Time 2 Crosstabulation

			Question 3 - time 2		
			No	**Yes**	**Total**
Question 3 -time 1	No	Count	17	5	22
		% of total	34.0%	10.0%	44.0%
	Yes	Count	6	22	28
		% of total	12.0%	44.0%	56.0%
Total		Count	23	27	50
		% of total	46.0%	54.0%	100.0%

Symmetric Measures

	Value	Asymp. std. error[a]	Approx. T[b]	Approx. sig.
Measure of agreement Kappa	0.556	0.118	3.933	0.000
N of valid cases	50			

[a] Not assuming the null hypothesis.

[b] Using the asymptotic standard error assuming the null hypothesis.

In the second Crosstabulation table, the percentage in agreement is 68% + 10%, or 0.78 as a proportion, and kappa is higher than in the first table at 0.337. Although the percentage in agreement in the third table is 34% + 44%, also 0.78 as a proportion, kappa is higher than in the second table at 0.556 and the *P* value increases in significance from 0.017 to <0.001. Thus, kappa varies for the same proportion in agreement. With a higher proportion of Yes replies (56% for question 3 compared with 22% for question 2), kappa increases from poor to moderate range.

A feature of kappa is that the value increases as the proportion of 'No' and 'Yes' responses become more equal and when the proportion in agreement remains the same. This feature is a major barrier to comparing kappa values. For this reason, the value of kappa, the percentage of positive responses and the proportion in agreement must all be reported to help assess repeatability.

Reporting the results

Information about the repeatability of the three questions can be reported as shown in Table 9.1. It is difficult to say which question is the most repeatable and has the least non-systematic bias because all three questions have a different percentage of positive responses and therefore the kappa values cannot be compared. However, both questions 2 and 3 have a higher proportion in agreement than question 1. The differences in percentages suggest that the three questions are measuring different entities.

Table 9.1 Repeatability for three questions administered to 50 people at a 3-week interval

	Percentage of positive responses at time 1	Percentage of positive responses at time 2	Proportion in agreement	Kappa
Question 1	30%	52%	0.62	0.25
Question 2	22%	20%	0.78	0.34
Question 3	56%	54%	0.78	0.56

Repeatability of continuous measurements

Continuous measurements must also have a high degree of repeatability to be useful as a research tool. Variations in continuous measurements can result from inconsistent measurement practices, from equipment variation or from ways in which results are read or interpreted. These sources can be measured as within-observer (intra-observer) variation, between-observer (inter-observer) variation or within-subject variation. Variations that result from the ways in which researchers administer, read or interpret tests are within- or between-observer variations. Variations that arise from patient compliance factors or from biological changes are within-subject variations. To quantify these measurement errors, the same measurement is taken from the same participant on two occasions or from the same participant by two observers and the results are compared.

Research question

The file **observer-weights.sav** contains data from 32 babies who had their weight measured by two nurses who had no knowledge of each other's measurements. The weights measured by both nurses could be plotted against each other in a scatter plot. However, it is best that a Pearson's correlation coefficient is not used to describe repeatability because it does not make sense to test the hypothesis that two measurements taken from the same babies using the same equipment are related to one another[2]. In addition, a second measurement that is, for example, twice as large as the first measurement would have perfect correlation but poor agreement.

To estimate the measurement error, the *Transform → Compute* command is first used to calculate the mean of the two measurements for each baby using the *Mean* function and then the difference between the two measurements as a simple subtraction, that is measurement 1 – measurement 2 is calculated with this command. The subtraction can be in either direction but the direction must be indicated in the summary results and graphs. The two new variables are created at the end of the data sheet and should be labelled as mean and differences respectively.

The size of the measurement error can then be calculated from the standard deviation around the differences, which can be obtained using the *Analyze → Descriptive Statistics → Descriptives* commands with the differences variable entered as the *Variable(s).*

Descriptives

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. deviation
Differences	32	−0.10	0.15	0.0125	0.06792
Valid *N* (listwise)	32				

The mean of the differences is 0.0125 and gives an estimate of the amount of bias between the two measurements. In this case, the measurements taken by nurse 1 are on average 0.0125 kg higher than nurse 2, which is a small difference. A problem with using the mean value is that large positive and large negative differences are balanced and therefore negated. However, the mean ± 1.96 SD can also be calculated from this table. This range is calculated as 0.0125 ± (1.96 × 0.0679), or −0.12 to 0.15 and is called the limits of agreement[3]. The limits of agreement indicate the interval in which 95% of the differences lie.

The mean and difference values can be plotted as a differences-vs-means plot to show whether the measurement error as estimated by the differences is related to the size of the measurement as estimated by the mean[4]. The shape of the scatter conveys important information about the repeatability of the measurements. A scatter that is evenly distributed above and below the zero line of no difference indicates that there is no systematic bias between the two observers. A scatter that is largely above or largely below the zero line of no difference or a scatter that increases or decreases with the mean value indicates a systematic bias between observers[5].

The values for the means and differences can be copied and pasted from SPSS to SigmaPlot and the figure can be created using the commands shown in Box 9.3. A recommendation for the axes of differences-vs-means plots is that the y-axis should be approximately one-third to one-half of the length of the x-axis[5].

Box 9.3 SigmaPlot commands to create a differences-vs-means plot

SigmaPlot Commands

SigmaPlot – [Data 1]*
Graph → Create Graph
Create Graph – Type
    Highlight Scatter Plot, click Next
Create Graph – Styles
    Highlight Simple Scatter, click Next
Create Graph – Data Format
    Under Data format, highlight XY pair, click Next
Create Graph – Select Data
    Highlight Column 1, click into Data for X
    Highlight Column 2, click into Data for Y
    Click Finish

The lines for the mean difference and limits of agreement can be added by typing the x coordinates in column 3 and y coordinates of the lines into columns 4 to 6 and adding three line plots by using the SigmaPlot commands *Graph → Add Plot → Line Plot → Simple Straight Line → XY Pair* options with x as column 3 each time and each y column. The columns for the coordinate data are as follows:

Column 3	Column 4	Column 5	Column 6
3.5	0.0125	−0.12	0.15
6.0	0.0125	−0.12	0.15

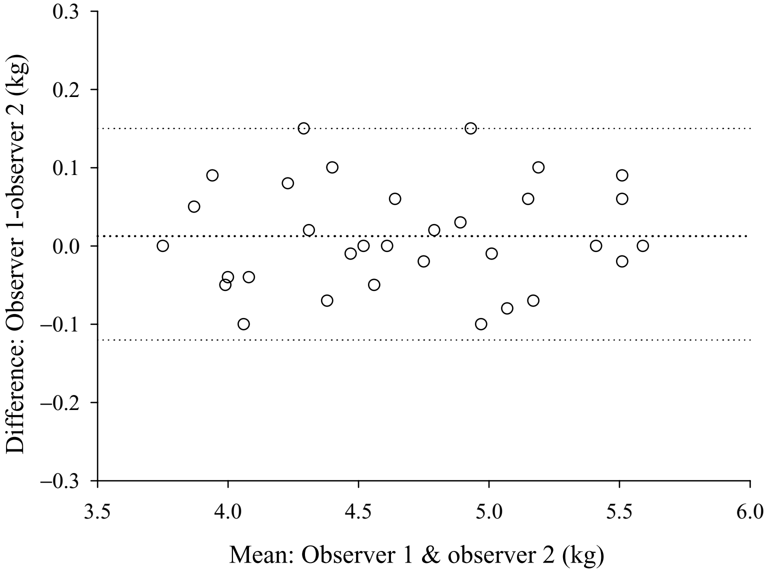

Figure 9.1 Differences-vs-means plot.

Figure 9.1 shows only a small amount of random error that is evenly scattered around the line of no difference and shows that most of the differences are within 0.1 kg. A wide scatter would indicate a large amount of measurement error. A Kendall's correlation coefficient between the means and the differences can be obtained using the commands shown in Box 6.3 in Chapter 6.

Non-parametric correlations

Correlations

			Differences	Mean
Kendall's tau_b	Differences	Correlation coefficient	1.000	0.045
		Sig. (two-tailed)	.	0.721
		N	32	32
	Mean	Correlation coefficient	0.045	1.000
		Sig. (two-tailed)	0.721	.
		N	32	32

The almost negligible correlation of 0.045 with a *P* value of 0.721 confirms the uniformity of variance in the repeated measurements. A systematic bias between the two measurements could be inspected using a paired *t*-test or a non-parametric rank sums test.

A more useful statistic to describe repeatability is to first calculate the measurement error from the standard deviation of the differences of observations in the same subject[3]. This is calculated as:

$$\begin{aligned}\text{Measurement error} &= \text{SD of differences}/\sqrt{2}\\ &= 0.06792/1.414\\ &= 0.048\ \text{kg}\end{aligned}$$

This error can then be converted to a range by multiplying by a critical value of 1.96.

$$\begin{aligned}\text{Error range} &= \text{Measurement error} \times \text{Critical value}\\ &= 0.048 \times 1.96\\ &= 0.09\ \text{kg}\end{aligned}$$

The error range indicates that the average of all possible measurements of a baby's weight is within the range of 0.09 kg above and 0.09 kg below the actual measurement taken. Thus for a baby with a measured weight of 4.01 kg, the average of all possible weights, which are expected to be close to the true weight, would be within the range 3.92 to 4.10 kg.

Intra-class correlation

The intra-class correlation coefficient (ICC) can be used to describe the relative extent to which two continuous measurements taken by different people or two measurements taken by the same person on different occasions are related. The advantage of ICC is that, unlike Pearson's correlation, a value of unity is only obtained when the two measurements are identical to one another. A high value of ICC of 0.95 indicates that 95% of the variance in the measurement is due to the true variance between the participants and 5% of the variance is due to measurement error or the variance within the participants or the observers. The SPSS commands to obtain ICC are shown in Box 9.4.

Box 9.4 SPSS commands to measure repeatability

SPSS Commands

observer-weights – SPSS Data Editor

Analyze → Scale → Reliability Analysis

Reliability Analysis

Highlight Weight–observer 1 and Weight–observer 2 and click into Items box

Click Statistics

Reliability Analysis: Statistics
Tick Intraclass correlation coefficient,
Model: Two-Way Mixed (default)
Type: Consistency (default)
Test Value: 0 (default), click Continue
Reliability Analysis
Click OK

Reliability

```
RELIABILITY ANALYSIS - SCALE (ALPHA)
                 Intraclass Correlation Coefficients
          Two-Way Mixed Effects Model (Consistency Definition)

                      ICC     95% Confidence Interval
Measure              Value   Lower Bound   Upper Bound F-Value Sig.

Single Rater         .9922     .9841         .9962     255.4797 .0000
Average of Raters*   .9961     .9920         .9981     255.4797 .0000

Degrees of freedom for F-tests are 31 and 31. Test Value = 0.

* Assumes absence of People*Rater interaction.

Reliability Coefficients

N of Cases =     32.0                   N of Items = 2
Alpha =    .9961
```

In this example, there are two raters (observers) and the ICC is 0.9961, that is less than 1% of the variance is explained by within-subject differences. The 95% confidence interval around an ICC is rarely used and the significance of the ICC is of no importance because it is expected that two measurements taken from the same person are highly related.

When reporting the results, the differences-vs-means plot gives the most informative description of agreement or repeatability. Additional information of the mean difference, the limits of agreement and the 95% range are direct measures of agreement between two continuous measurements whereas the intra-class correlation coefficient is a relative measure of agreement. All of these statistics should be included when reporting information of the agreement or repeatability between two measurements because they all convey relevant information.

Notes for critical appraisal

Paired measurements to estimate agreement must be treated appropriately when analysing the data. When critically appraising an article that presents these types of statistics, it is important to ask the questions shown in Box 9.5.

Box 9.5 Questions for critical appraisal

The following questions should be asked when appraising published results from paired categorical follow-up data or data collected to estimate the repeatability of questionnaire responses or continuous measurements:

- Is the sample size large enough to have confidence in the summary estimates?

For repeatability of categorical data:

- Is the percentage of positive or negative responses and proportion in agreement included in addition to kappa?
- Are kappa values inappropriately compared?

For repeatability of continuous measurements:

- Have a differences-vs-means plot, the limits of agreement, a 95% range and the intra-class correlation been reported?
- Is Pearson's correlation used inappropriately?

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CHAPTER 10
Categorical and continuous variables: diagnostic statistics

Like dreams, statistics are a form of wish fulfilment.
JEAN BAUDRILLARD (b. 1929), FRENCH SEMIOLOGIST

Objectives

The objectives of the chapter are to explain how to:

- compute sensitivity, specificity and likelihood ratios
- understand the limitations of positive and negative predictive values
- select cut-off points for screening and diagnostic tests
- critically appraise studies that use or evaluate diagnostic tests

In clinical practice it is important to know how well diagnostic tests, such as x-rays, biopsies or blood and urine tests, can predict that a patient has a certain condition or disease. The statistics positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity are all used to estimate the utility of a test in predicting the presence of a condition or a disease. A statistic that combines the utility of sensitivity and specificity is the likelihood ratio (LR). If the outcome of the diagnostic test is binary, a likelihood ratio can be calculated directly. If the test result is on a continuous scale, a receiver operating characteristic (ROC) curve is used to determine the point that maximises the LR.

Diagnostic statistics are part of a group of statistics used to describe agreement between two measurements. However, these statistics should only be calculated when there is a 'gold standard' to measure the presence or absence of disease against which the test can be compared. If a gold diagnostic standard does not exist, a proxy gold standard may need to be justified[1]. In this situation, the test being evaluated must not be included in the definition of the gold standard[1]. In measuring the diagnostic utility of a test, the person interpreting the test measurement must have no knowledge of the disease status of each patient.

Coding

For diagnostic statistics, it is best to code the variable indicating disease status as 1 for disease present as measured by the gold standard or test positive and

2 for disease absent or test negative. This coding will produce a table with the rows and columns in the order shown in Table 10.1. In this table, the row and column order is the reverse of that used to calculate an odds ratio from a 2 × 2 crosstabulation but is identical to the coding shown in Table 8.1 in Chapter 8 which is frequently used in clinical epidemiology textbooks.

Table 10.1 Coding for diagnostic statistics

	Disease present	Disease absent	Total
Test positive	a	b	$a+b$
Test negative	c	d	$c+d$
Total	$a+c$	$b+d$	N

Positive and negative predictive values

In estimating the utility of a test, PPV is the proportion of patients who are test positive and in whom the disease is present and NPV is the proportion of patients who are test negative and in whom the disease is absent. These statistics indicate the probability that the test will make a correct diagnosis[2]. Both PPV and NPV are statistics that predict from the test to the disease and indicate the probability that patients will or will not have a disease if they have a positive or negative diagnostic test. Intuitively, it would seem that PPV and NPV would be the most useful statistics; however, they have serious limitations in their interpretations[2].

The statistics PPV and NPV should only be calculated if the study sample is from a population and not if groups of patients and healthy people are recruited independently, which is often the case. From Table 10.1, the PPV and NPV can be calculated as follows:

$$\text{PPV} = a/(a+b)$$
$$\text{NPV} = d/(c+d)$$

Research question

The file **xray.sav** contains the data from 150 patients who had an x-ray for a bone fracture. A positive x-ray means that a fracture appears to be present on the x-ray, and a negative x-ray means that there is no indication of a fracture on the x-ray. The presence or absence of a fracture was later confirmed during surgery. Thus surgery is the ‘gold standard’ for deciding whether or not a fracture was present. The research question is how accurate are x-rays in predicting fractures in people. In computing diagnostic statistics, a hypothesis is not being tested so that the *P* value for the crosstabulation has little meaning.

Diagnostic statistics of PPV and NPV are computed using the SPSS commands shown in Box 10.1 with row percentages requested because PPV and NPV are calculated as proportions of the test positive patients and test negative patients who have the disease. In SPSS, PPV and NPV are not produced directly or labelled as such but can be simply derived from the row percentages. Although the figures are given in percentages, diagnostic statistics are more commonly reported as proportions, that is, in decimal form.

Box 10.1 SPSS commands to compute diagnostic statistics

SPSS Commands

xray - SPSS Data Editor
Analyze → Descriptive Statistics → Crosstabs
Crosstabs
    Highlight Xray results (test) and click into Row(s)
    Highlight Fracture detected by surgery (disease) and click into Column(s)
    Click on Statistics
Crosstabs: Statistics
    Check all boxes are empty, click Continue
Crosstabs
    Click on Cells
Crosstabs: Cell Display
    Under Percentages tick Row, tick Continue
    Click OK

Crosstab

X-ray Results * Fracture Detected by Surgery Crosstabulation

			Fracture detected by surgery (disease)		
			Present	**Absent**	**Total**
X-ray results (test)	Positive	Count	36	24	60
		% within x-ray results	60.0%	40.0%	100.0%
	Negative	Count	8	82	90
		% within x-ray results	8.9%	91.1%	100.0%
Total		Count	44	106	150
		% within x-ray results	29.3%	70.7%	100.0%

From the crosstabulation the row percentages are used and are simply converted to a proportion by dividing by 100.

Positive predictive value = 0.60 (i.e. 36/60)

Negative predictive value = 0.91 (i.e. 82/90)

This indicates that 0.60 of patients who had a positive x-ray had a fracture and 0.91 who had a negative x-ray did not have a fracture.

To measure the certainty of diagnostic statistics, confidence intervals for PPV and NPV can be calculated as for any proportion. If the confidence interval around a proportion contains a value less than zero, exact confidence intervals based on the binomial distribution should be used rather than asymptotic statistics based on a normal distribution[3]. The formula for calculating the standard error around a proportion was shown in Chapter 7. The Excel spreadsheet shown in Table 10.2 can be used to calculate 95% confidence intervals for PPV and NPV. The confidence interval for PPV is based on the total number of patients who have a positive test result and the confidence interval for NPV is based on the total number of patients who have a negative test result.

Table 10.2 Excel spreadsheet to calculate 95% confidence intervals

	Proportion	*N*	SE	Width	CI lower	CI upper
PPV	0.6	60	0.063	0.124	0.476	0.724
NPV	0.91	90	0.030	0.059	0.851	0.969

The interpretation of the 95% confidence interval for PPV is that with 95% confidence, 47.6% to 72.4% of patients with a positive x-ray will have a fracture. The interpretation of the 95% confidence interval for NPV is that with 95% confidence, 85.1% to 96.9% of patients with a negative x-ray will not have a fracture. Confidence intervals should be interpreted taking the sample size into account. The larger the sample size, the narrower the confidence intervals will be.

Although PPV and NPV seem intuitive to interpret, both statistics vary with changes in the proportion of patients in the sample who are disease positive. Thus, these statistics can only be applied to the study sample or to a sample with the same proportion of disease positive and disease negative patients. For this reason, PPV and NPV are not commonly used in clinical practice. Box 10.2 shows why these statistics are limited in their interpretation.

Box 10.2 Limitations in the interpretation of positive and negative predictive values

Positive and negative predictive values:

- are strongly influenced by the proportion of patients who are disease positive
- increase when the per cent of patients who have the disease in the sample is high and decrease when the per cent who have the disease is small
- cannot be applied or generalised to other clinical settings with different patient profiles
- cannot be compared between different diagnostic tests

In practice, the statistics PPV and NPV are only useful in settings in which the per cent of patients who have the disease present is the same as the prevalence of the disease in the population. This naturally rules out most clinical settings.

Sensitivity and specificity

The statistics that are most often used to describe the utility of diagnostic tests in clinical applications are sensitivity, specificity[4] and likelihood ratio[5]. These diagnostic statistics can be computed from Table 10.1 as follows:

Sensitivity $= a/(a + c)$
Specificity $= d/(b + d)$
Likelihood ratio $=$ Sensitivity$/(1 -$ specificity$)$

Sensitivity indicates how likely patients are to have a positive test if they have the disease and specificity indicates how likely the patients are to have a negative test if they do not have the disease. In this sense, these two statistics describe the proportion of patients in each disease category who are test positive or negative. Although the usefulness of these statistics is not as intuitive, sensitivity and specificity have advantages over PPV and NPV as shown in Box 10.3.

Box 10.3 Advantages of using sensitivity and specificity to describe the application of diagnostic tests

The advantages of using sensitivity and specificity to describe diagnostic tests are that these statistics:

- do not alter if the prevalence of disease is different between clinical populations
- can be applied in different clinical populations and settings
- can be compared between studies with different inclusion criteria
- can be used to compare the diagnostic potential of different tests

The interpretation of sensitivity and specificity is not intuitive and therefore to calculate these statistics it is recommended that the notations of true positives (TP), false positives (FP), true negatives (TN) and false negatives (FN) are written in each quadrant of crosstabulation as shown in Table 10.3. The false negative group is the proportion of patients who have the disease and who have a negative test result. The false positive group is the proportion of patients who do not have the disease and who have a positive test result.

Thus, sensitivity is the rate of true positives in the disease-present group ($a/a + c$) and specificity is the rate of true negatives in the disease-absent group ($d/b + d$). The 'opposites' rule applies to remembering the meaning of the terms sensitivity and specificity because: sensitivity has a 'n' in it and this

Table 10.3 Terms used in diagnostic statistics

	Disease present	**Disease absent**	**Total**
Test positive	a TP (sensitivity) (true +ve)	b FP (false +ve)	
Test negative	c FN (false −ve)	d TN (specificity) (true −ve)	
Total	$a + c$	$b + d$	N

applies to the true positives, which begin with ‘p’ and specificity has a ‘p’ in it and this applies to the true negatives, which begin with ‘n’.

Is this logical? Well no, but the terminology is well established and this reverse code helps in remembering which term indicates the true negatives or true positives. From Table 10.3 it can be seen that the rate of false negatives is the complement of the true positives for patients who have the disease. Similarly, the rate of false positives is the complement of the true negatives for patients who do not have the disease.

SpPin and SnNout

SpPin and SnNout are two clinical epidemiology terms that are commonly used to aid in the interpretation of sensitivity and specificity in clinical settings[6].

SpPin stands for **Sp**ecificity**-P**ositive**-in,** which means that if a test has a high specificity (TN) and therefore a low 1 – specificity (FP), a positive result rules the disease in. A test that is used to diagnose an illness in patients with symptoms of the illness needs to have a low false positive rate because it will then identify most of the people who do not have the disease. Although specificity needs to be high for a diagnostic test to rule the disease in, it is calculated solely from patients without the disease.

SnNout stands for **S**e**n**sitivity**-N**egative**-out**, which means that if the test has a high sensitivity (TP) and a low 1 – sensitivity (FN), a negative test result rules the disease out. A test that is used to screen a population in which many people will not have the disease needs to have high sensitivity because it will then identify all of the people with the disease. Although sensitivity needs to be high in a screening test to rule the disease out, it is calculated solely from patients with the disease.

The SPSS commands shown in Box 10.1 can be used to compute sensitivity and specificity but the column percentages rather than the row percentages are requested because sensitivity is a proportion of the disease positive group and specificity is a proportion of the disease negative group.

Crosstab

X-ray Results * Fracture Detected by Surgery Crosstabulation

			Fracture detected by surgery (disease)		
			Present	**Absent**	**Total**
X-ray results (test)	Positive	Count	36	24	60
		% within fracture detected by surgery	81.8%	22.6%	40.0%
	Negative	Count	8	82	90
		% within fracture detected by surgery	18.2%	77.4%	60.0%
Total		Count	44	106	150
		% within fracture detected by surgery	100.0%	100.0%	100.0%

The column percentages can be simply changed into proportions by dividing by 100. Thus, from the above table:

$$\begin{aligned} \text{Sensitivity} &= \text{TP} = 0.82 \\ 1 - \text{sensitivity} &= \text{FN} = 0.18 \\ \text{Specificity} &= \text{TN} = 0.77 \\ 1 - \text{specificity} &= \text{FP} = 0.23 \end{aligned}$$

The sensitivity of the test indicates that 82% of patients with a fracture will have a positive x-ray and the specificity of the test indicates that 77.4% of patients with no fracture will have a negative x-ray.

Confidence intervals

The confidence intervals for sensitivity and specificity can be calculated using the spreadsheet shown in Table 10.2. This produces the intervals shown in Table 10.4. Again, if the confidence interval of a proportion contains a value less than zero, exact confidence intervals should be used[3].

Table 10.4 Excel spreadsheet for calculating confidence intervals around a proportion

Proportion	*N*	SE	Width	CI lower	CI upper
0.82	44	0.058	0.114	0.706	0.934
0.18	44	0.058	0.114	0.066	0.294
0.77	106	0.041	0.080	0.690	0.850
0.23	106	0.041	0.080	0.150	0.310

These 95% confidence intervals are based on the number of patients with the disease present for sensitivity and the number of patients with the disease absent for specificity. Because each 95% confidence interval is based on only a subset of the sample rather than on the total sample size, the confidence intervals can be surprisingly wide if the number in the group is quite small.

The interpretation of the intervals for sensitivity is that with 95% confidence between 70.6% and 93.4% of patients with a fracture will have a positive x-ray. Similarly, the interpretation for specificity is that with 95% confidence between 69.0% and 85% of patients without a fracture will have a negative x-ray.

Study design

In calculating the required sample size to estimate sensitivity and specificity, it is important to have an adequate number of people with and without the disease. A high sensitivity rules the disease out, therefore it is essential to enrol a large number of people with disease present to calculate the proportion of true positives with precision. A high specificity rules the disease in, so it is essential to enrol a large number of people with the disease absent to calculate the proportion of true negatives with precision.

It is not always understood that to show that a test can rule a disease out, a large number of people with the disease present must be enrolled and that to show that a test is useful in ruling a disease in, a large number of people without the disease must be enrolled. For most tests, a large number of people with the disease present and with the disease absent must be enrolled to provide tighter confidence intervals around both sensitivity and specificity.

Likelihood ratio

Both sensitivity and specificity can be thought of as statistics that ‘look backwards’ in that they show the probability that a person with a disease will have a positive test rather than looking ‘forwards’ and showing the probability that the person who tests positive has the disease. Also, sensitivity and specificity should not be used in isolation because each is calculated from separate parts of the data. To be useful in clinical practice, these statistics need to be converted to a likelihood ratio that uses data from the total sample to estimate the relative predictive value of the test. The LR is calculated as follows:

$$\begin{aligned}\text{LR} &= \frac{\text{Likelihood of a positive result in people with disease}}{\text{Likelihood of a positive result in people without disease}}\\ &= \text{Sensitivity}/(1-\text{specificity})\\ &= \text{TP}/\text{FP}\end{aligned}$$

The LR is simply the ratio of true positives to the false positives and indicates how likely a positive result will be found in a person with the disease than in a person without the disease[1]. From the previous calculation:

$$\text{LR} = 0.82/(1 - 0.77) = 3.56$$

Confidence intervals around LR are best generated using dedicated programs (see useful websites). The LR indicates how much a positive test will alter the pre-test probability that a patient will have the illness. The pre-test probability is the probability of the disease in the clinic setting where the test is being used. The post-test probability is the probability that the disease is present when the test is positive. To interpret the LR, a likelihood ratio nomogram can be used to convert pre-test probability of disease into post-test probability[3, 7]. Alternatively, the following formula can be used to convert the pre-test probability (Pre-TP) into a post-test probability (Post-TP):

$$\text{Post-TP} = (\text{Pre-TP} \times \text{LR})/(1 + \text{Pre-TP} \times (\text{LR} - 1))$$

The size of the LR indicates the utility of the test in diagnosing an illness. As a rule, a LR greater than 10 is large and means a conclusive change from pre-test to post-test probability. On the other hand a LR between 5 and 10 results in only a moderate shift between pre- and post-test probability, a LR between 2 and 5 results in a small shift but sometimes reflects an important shift, and a LR below 2 is small and rarely important[4].

The advantages of using a likelihood ratio to interpret the results of diagnostic tests are shown in Box 10.4.

Box 10.4 Advantages of using likelihood ratio as a predictive statistic for diagnostic tests

The advantages of likelihood ratio are that this predictive statistic:

- allows valid comparisons of diagnostic statistics between studies
- the diagnostic value can be applied in different clinical settings
- provides the certainty of a positive diagnosis

ROC curves

Receiver operating characteristic (ROC) curves are an invaluable tool for finding the cut-off point in a continuously distributed measurement that best predicts whether a condition is present, for example whether patients are disease positive or disease negative[8]. ROC curves are used to find a cut-off value that delineates a ‘normal’ from an ‘abnormal’ test result when the test result is a continuously distributed measurement. ROC curves are plotted by calculating the sensitivity and specificity of the test in predicting the diagnosis for each value of the measurement. The curve makes it possible to determine a cut-off point for the measurement that maximises the rate of true positives (sensitivity) and minimises the rate of false positives (1 – specificity), and thus maximises the likelihood ratio.

Research question

The file **xray.sav**, which was used in the previous research question, also contains data for the results of three different biochemical tests and a variable that indicates whether the disease was later confirmed by surgery. ROC curves are used to assess which test is most useful in predicting that patients will be disease positive.

Before constructing a ROC curve, the amount of overlap in the distribution of the continuous biochemical test measurement in both the disease positive and disease negative groups can be explored using the SPSS commands shown in Box 10.5.

Box 10.5 SPSS commands to obtain scatter plots

SPSS Commands

xray - SPSS Data Editor

  Graphs → Scatter

Scatterplot

  Click on Simple, click on Define

Simple Scatterplots

  Highlight BiochemA and click into the Y Axis

  Highlight Disease positive and click into the X Axis

  Click OK

These SPSS commands can be repeated to obtain scatter plots for the test BiochemB and BiochemC as shown in Figure 10.1. In the plots, the values and labels on the *x*- and *y*-axes are automatically assigned by SPSS and are not selected labels. For example, in Figure 10.1 the tests are never negative as suggested by the negative values on the *y*-axis and the group labels of 1 for disease present and 2 for disease absent on the *x*-axis are not displayed. Although the scatter plots are useful for understanding the discriminatory value of each continuous variable, they would not be reported in a journal article.

In the first plot shown in Figure 10.1, it is clear that the values for BiochemA in the disease positive group (coded 1) overlap almost completely with the values for BiochemA in the disease negative group (coded 2). With complete overlap such as this, there will never be a cut-off point that effectively delineates between the two groups.

In the plots for BiochemB and BiochemC as shown in Figure 10.1, there is more separation of the test measurements between the groups, particularly for BiochemC. The value of the tests in distinguishing between the disease positive and disease negative groups can be quantified by plotting ROC curves using the commands shown in Box 10.6. In the data set, disease positive is coded as 1 and this value is entered into the State Variable box.

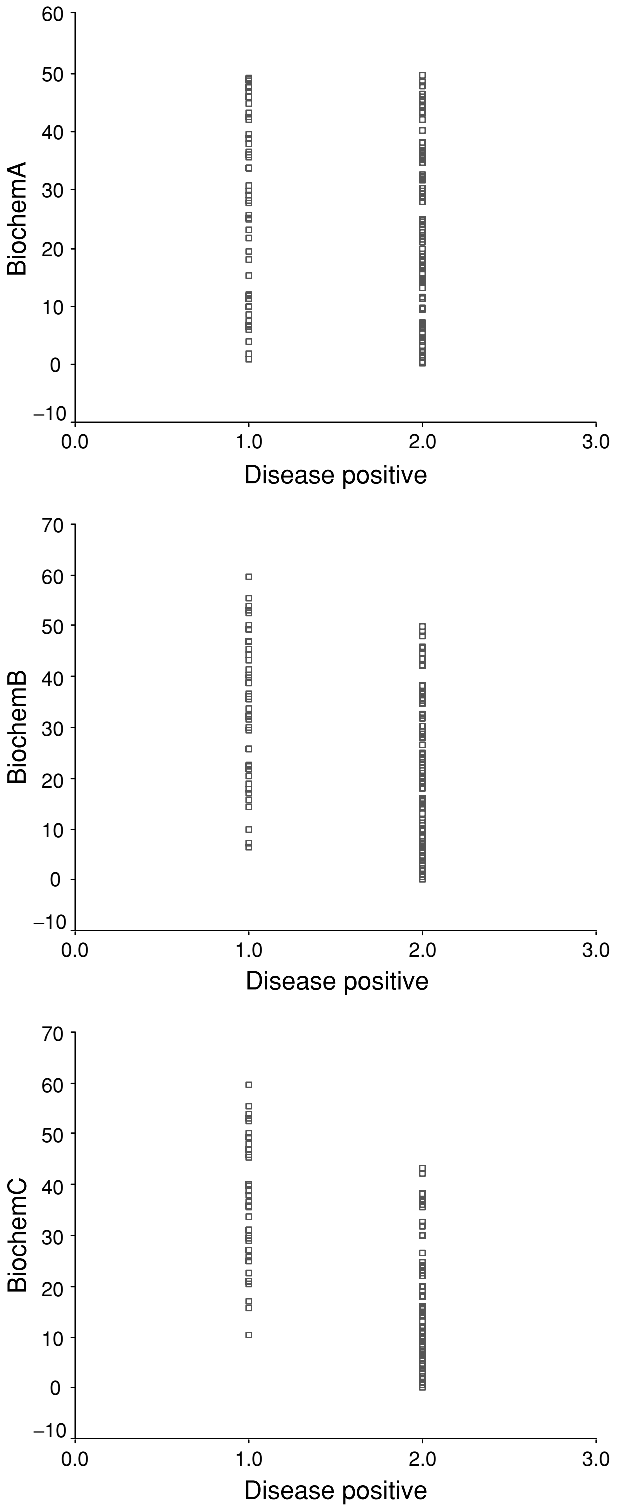

Figure 10.1 Scatter plots for BiochemA, B and C by disease status.

Box 10.6 SPSS commands to plot a ROC curve

SPSS Commands

xray - SPSS Data Editor
Graphs → ROC Curve
ROC Curve
   Highlight BiochemA, BiochemB and BiochemC and click into Test Variable
   Highlight Disease positive and click into State Variable
   Type in 1 as Value of State Variable
   Under Display tick ROC Curve (default), With diagonal reference line, and Standard error and confidence interval
   Click OK

Area Under the Curve

				Asymptotic 95% confidence interval	
Test result varible(s)	**Area**	**Std. error**[a]	**Asymptotic sig.**[b]	**Lower bound**	**Upper bound**
BiochemA	0.580	0.051	0.114	0.479	0.681
BoichemB	0.755	0.042	0.000	0.673	0.837
BiochemC	0.886	0.028	0.000	0.832	0.940

[a] Under the non-parametric assumption.

[b] Null hypothesis: true area = 0.5.

In a ROC curve, sensitivity is calculated using every value of BiochemA in the data set as a cut-off point and is plotted against the corresponding 1 – specificity at that point, as shown in Figure 10.2. Thus the curve is the true positives plotted against the false positives calculated using each value of the test as a cut-off point. In Figure 10.2, the diagonal line indicates where the test would fall if the results were no better than chance at predicting the presence of a disease, that is no better than tossing a coin. BiochemA lies close to this line confirming that the test is poor at discriminating between disease positive and disease negative patients.

The area under the diagonal line is 0.5 of the total area. The greater the area under the ROC curve, the more useful the measurement is in predicting the patients who have the disease. A curve that falls substantially below the diagonal line indicates that the test is useful for predicting patients who do not have the disease.

The Area Under the Curve table indicates that the area under the curve for BiochemA is 0.580 with a non-significant *P* value (asymptotic significance) of 0.114, which shows that the area is not significantly different from 0.5. The 95% confidence intervals contain the value 0.5 confirming the *P* value that shows that this test is not a significant predictor of disease status.

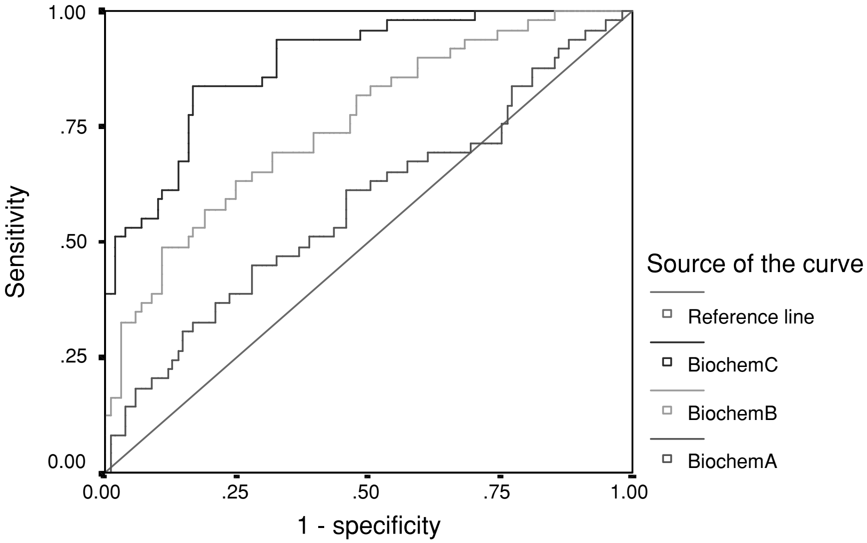

Figure 10.2 ROC curves for Biochem A, B and C.

The ROC curves in Figure 10.2 show that, as expected from the previous scatter plots, the tests BiochemB and BiochemC detect the disease positive patients more effectively than BiochemA. In the Area under the Curve table, BiochemC is the superior test because the area under its ROC curve is the largest at 0.886. Both BiochemB and BiochemC have an area under the curve that is significantly greater than 0.5 and in both cases, the *P* value is <0.0001. The very small amount of overlap of confidence intervals between BiochemB and BiochemC suggests that BiochemC is a significantly better diagnostic test than BiochemB, even though the *P* values are identical.

The choice of the cut-off point that optimises the utility of the test is often an expert decision taking factors such as the sensitivity, specificity, cost and purpose of the test into account. In diagnosing a disease, the gold standard test may be a biopsy or surgery, which is invasive, expensive and carries a degree of risk, for example the risk of undergoing an anaesthetic. Tests that are markers of the presence or absence of disease are often used to reduce the number of patients who require such invasive interventions. The exact points on the curve that are selected as cut-off points will vary according to each situation and are best selected using expert opinion.

Three different cut-off points on the curve are used for a diagnostic test, a general optimal test and a screening test. The cut-off point for a screening test is chosen to maximise the sensitivity of the test and for a diagnostic test is chosen to maximise the specificity of the test. The cut-off point for a general optimal test is chosen to optimise the rate of true positives whilst minimising the rate of false positives. All three points can be identified from the coordinates of the ROC curve. By entering only BiochemC into the Test Variable box of *Graphs → ROC* and ticking the box ‘Coordinate Points of the ROC Curve’ the

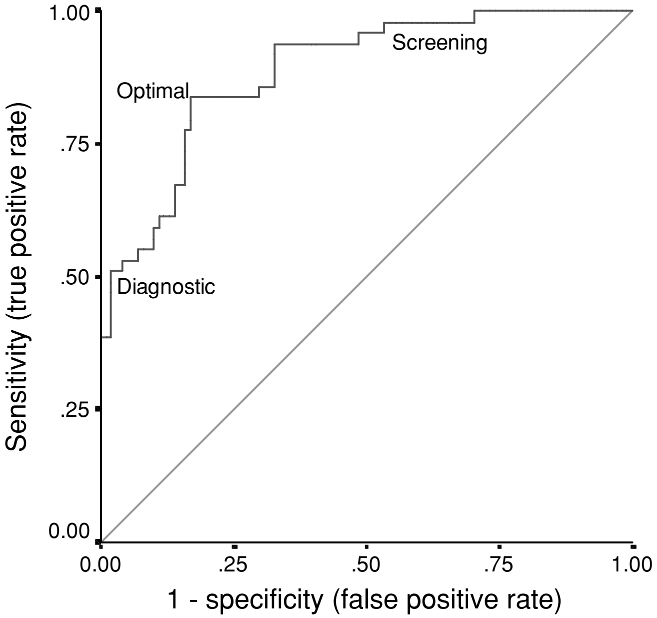

Figure 10.3 ROC curve for BiochemC with diagnostic, optimal and screening cut-off points.

ROC curve and a list of the points on the graph are printed as shown in Figure 10.3.

The cut-off point for a *general optimal test*, which is sometimes called the optimal diagnostic point, is the point on the curve that is closest to the top of the left hand *y*-axis. This point is shown in Figure 10.3 and the test cut-off value can be identified from the coordinate points of the curve. The coordinate points from the central section of the SPSS output have been copied to an Excel spreadsheet and are shown in Table 10.5. In the table, the Excel function option has been used to also calculate Specificity and 1 – sensitivity for each point.

To find the coordinates of the optimal diagnostic point, a simple method is to use a ruler to calculate the coordinate value for 1 – specificity of the optimal cut-off point. Once the point is identified on the graph as being the closest point to the top of the *y*-axis on the ROC curve, a line can be drawn vertically down to the *x*-axis. The value for 1 – specificity is then calculated as the ratio of the distance of the point from the *y*-axis to the total length of the *x*-axis. Using this method, this value is estimated to be 0.167. In the '1 – specificity' column of Table 10.5, there are three values of 0.168, which are closest to 0.167. For the first value of 0.168, sensitivity equals 0.837 after which it begins to fall to 0.796 and 0.776. Thus, of the three points, the first point optimises sensitivity while 1 – specificity remains constant at 0.168. At this value, specificity is 1 – 0.168, or 0.832. The value of BiochemC at this coordinate is 24.8, which is the cut-off point for an optimal general test or is the optimal diagnostic point.

Table 10.5 Excel spreadsheet to identify clinical cut-off points

Cut-off point	Sensitivity True positives	1 – specificity False positives	Specificity True negatives	1 – sensitivity False negatives	Distance
14.950	0.980	0.584	0.416	0.020	0.342
15.150	0.980	0.564	0.436	0.020	0.319
15.350	0.980	0.554	0.446	0.020	0.308
15.550	0.980	0.545	0.455	0.020	0.297
15.750	**0.980**	**0.535**	**0.465**	**0.020**	**0.286**
15.900	0.959	0.535	0.465	0.041	0.288
16.500	0.959	0.485	0.515	0.041	0.237
17.500	0.939	0.485	0.515	0.061	0.239
18.450	0.939	0.406	0.594	0.061	0.169
19.450	0.939	0.396	0.604	0.061	0.161
20.200	0.939	0.327	0.673	0.061	0.111
20.700	0.918	0.327	0.673	0.082	0.113
21.500	0.857	0.327	0.673	0.143	0.127
22.300	0.857	0.297	0.703	0.143	0.109
22.650	0.837	0.297	0.703	0.163	0.115
22.850	0.837	0.287	0.713	0.163	0.109
23.500	0.837	0.228	0.772	0.163	0.079
24.050	0.837	0.188	0.812	0.163	0.062
24.350	0.837	0.178	0.822	0.163	0.058
24.800	**0.837**	**0.168**	**0.832**	**0.163**	**0.055**
25.400	0.796	0.168	0.832	0.204	0.070
26.150	0.776	0.168	0.832	0.224	0.079
26.750	0.776	0.158	0.842	0.224	0.075
28.000	0.735	0.158	0.842	0.265	0.095
29.200	0.714	0.158	0.842	0.286	0.107
29.650	0.694	0.158	0.842	0.306	0.119
29.950	0.673	0.158	0.842	0.327	0.132
30.500	0.673	0.139	0.861	0.327	0.126
31.400	0.612	0.139	0.861	0.388	0.170
31.850	0.612	0.129	0.871	0.388	0.167
32.300	0.612	0.119	0.881	0.388	0.164
33.200	0.612	0.109	0.891	0.388	0.162
34.600	0.592	0.109	0.891	0.408	0.178
35.550	0.592	0.099	0.901	0.408	0.176
35.650	0.571	0.099	0.901	0.429	0.193
35.900	0.551	0.099	0.901	0.449	0.211
36.350	0.551	0.079	0.921	0.449	0.208
36.650	0.551	0.069	0.931	0.449	0.206
36.800	0.531	0.069	0.931	0.469	0.225
37.050	0.531	0.050	0.950	0.469	0.223
37.600	0.531	0.040	0.960	0.469	0.222
38.100	0.510	0.040	0.960	0.490	0.241

Continued

Table 10.5 *(Conitnued)*

Cut-off point	Sensitivity True positives	1 – specificity False positives	Specificity True negatives	1 – sensitivity False negatives	Distance
38.500	**0.510**	**0.020**	**0.980**	**0.490**	**0.240**
38.250	0.510	0.030	0.970	0.490	0.241
39.200	0.490	0.020	0.980	0.510	0.261
39.850	0.469	0.020	0.980	0.531	0.282
41.100	0.388	0.020	0.980	0.612	0.375
42.700	0.388	0.010	0.990	0.612	0.375
44.250	0.388	0.000	1.000	0.612	0.375

An alternative method to identify the cut-off point from the Excel spreadsheet is to use the following arithmetic expression, which uses Pythagoras' theorem, to identify the distance of each point from the top of the y-axis. In this calculation, the 'distance' has no units but is a relative measure:

$$\text{Distance} = (1 - \text{Sensitivity})^2 + (1 - \text{Specificity})^2$$

This value was calculated for all points in Table 10.5 using the function option in Excel. The minimum distance value is 0.055 for the cut-off point 24.8. Above and below this value the distance increases indicating that the points are further from the optimal diagnostic point. When the point closest to the top of the y-axis is not readily identified from the ROC curve, this method is useful for identifying the cut-off value.

The cut-off points that would be used for diagnostic and screening tests can also be read from the ROC curve coordinates. For a diagnostic test, it is important to maximise specificity while optimising sensitivity. From the ROC curve figure, the value that would be used for a *diagnostic test* is where the curve is close to the left hand axis, that is where the rate of false positives (1 – specificity) is low and thus the rate of true negatives (specificity) is high. At the cut-off point where the test value is 38.5, there is a sensitivity of 0.510 and a low 1 – specificity of 0.02. At this test value, specificity is high at 0.98 which is a requirement for a diagnostic test. Ideally, specificity should be 1.0 but this has to be balanced against the rate of true positives. At the three test values that have the same sensitivity of 0.510, the rate of false positive is higher for the cut-off points of 38.1 and 38.25 than for the cut-off point of 38.5, which maximises specificity while optimising sensitivity. At the cut-off points below 38.5 where specificity is also 0.98, a significant reduction in true positives would occur if the cut-off point of 41.10 with a sensitivity of 0.388 was selected.

The value that would be used for a *screening test* is where the curve is close to the top axis where the rate of true positives (sensitivity) is maximised. For a screening test, it is important to maximise sensitivity while optimising specificity. At the cut-off point where the test value is 15.75, a high sensitivity of 0.98 is attained for a specificity of 0.465 (Table 10.5). At this point the false negative rate (1 – sensitivity) is low at 0.02 which is a requirement of a screening test. Ideally, sensitivity should be 1.0 but this has to be balanced against the rate of false positives. The original SPSS output (not shown here) indicates that there are 13 test values below 15.75 at which sensitivity remains constant at 0.980 but there is a large gain in the rate of false positives across these cut-off points from 0.535 to 0.703. Thus, at several cut-off values below 15.75, specificity decreases for no change in sensitivity.

For all three cut-off points, the choice of a cut-off value needs to be made using expert opinion in addition to the ROC curve. In this, the decision needs to be made about how important it is to minimise the occurrence of false negative or false positive results.

Reporting the results

The results from the above analyses could be reported as shown in Table 10.6. The positive likelihood ratio is computed for each cut-off point as sensitivity/1 – specificity. A high positive likelihood ratio is more important for a diagnostic test than for a screening test. The 95% confidence intervals for sensitivity and specificity are calculated using the Excel spreadsheet in Table 10.2 with the numbers of disease positive (49) and disease negative (101) patients respectively used as the sample sizes.

Table 10.6 Cut-off points and diagnostic utility of test BiochemC for identifying disease positive patients

Purpose	Cut-off value	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio
Screening	15.8	0.98 (0.94, 1.02)	0.47 (0.37, 0.57)	1.8
Optimal	24.8	0.84 (0.74, 0.94)	0.83 (0.76 to 0.90)	4.9
Diagnostic	38.5	0.51 (0.37, 0.65)	0.98 (0.95, 1.0)	25.5

Notes for critical appraisal

When critically appraising an article that presents information about diagnostic tests, it is important to ask the questions shown in Box 10.7. In diagnostic tests, 95% confidence intervals are rarely reported but knowledge of the precision around measurements of sensitivity and specificity is important for applying the test in clinical practice. In addition, estimating sample size in the disease positive and negative groups is of paramount importance in designing studies to measure diagnostic statistics with accuracy.

Box 10.7 Questions for critical appraisal

The following questions should be asked when appraising studies from which diagnostic statistics are reported:

- Was a standard protocol used for deciding whether the diagnosis and the test were classified as positive or negative?
- Was a gold standard used to classify the diagnosis?
- Was knowledge of the results of the test witheld from the people who classified patients as having a disease and vice versa?
- How long was the time interval between the test and the diagnosis? Could the condition have changed through medication use, natural progression, etc. during this time?
- Are there sufficient disease positive and disease negative people in the sample to calculate both sensitivity and specificity accurately?
- Have confidence intervals been calculated for sensitivity and specificity?

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CHAPTER 11
Categorical and continuous variables: survival analyses

The individual source of the statistics may easily be the weakest link. Harold Cox tells a story of his life as a young man in India. He quoted some statistics to a judge who was an Englishman. The judge said, Cox, when you are a bit older, you will not quote Indian statistics with that assurance. The Government are very keen on amassing statistics—they collect them, add them, raise them to the nth power, take the cube root and prepare wonderful diagrams. But what you must never forget is that every one of those figures comes in the first instance from the chowkidar (village watchman), who just puts down whatever he pleases.

JOSIAH CHARLES STAMP (1880 – 1941)

Objectives

The objectives of the chapter are to explain how to:
- decide when survival analyses are appropriate
- obtain and interpret the results of survival analyses
- ensure that the assumptions for survival analyses are met
- report results in a graph or a table
- critically appraise the survival analyses reported in the literature

Survival analyses are used to investigate the time between entry into a study and the subsequent occurrence of an event. Although survival analyses were designed to measure differences between time to death in study groups, they are frequently used for time to other events including discharge from hospital; disease onset; disease relapse or treatment failure; or cessation of an activity such as breastfeeding or use of contraception.

With data relating to time, a number of problems occur. The time to an event is rarely normally distributed and follow-up times for patients enrolled in cohort studies vary, especially when it is impractical to wait until the event has occurred in all patients. In addition, patients who leave the study early or who have had less opportunity for the event to occur need to be taken into account. Survival analyses circumvent these problems by taking advantage of the longitudinal nature of the data to compare event rates over the study period and not at an arbitrary time point[1].

Survival analyses are ideal for analysing event data from prospective cohort studies and from randomised controlled trials in which patients are enrolled in the study over long time periods. The advantages of using survival analyses rather than logistic regression for measuring the risk of the event occurring are that the time to the event is used in the analysis and that the different length of follow-up for each patient is taken into account. This is important because a patient in one group who has been enrolled for only 12 months does not have an equal chance for the event to occur as a patient in another group who has been enrolled for 24 months. Survival analyses also have an advantage over regression in that the event rate over time does not have to be constant.

Censored observations

Patients who leave the study or do not experience the event are called 'censored' observations. The term censoring is used because, in addition to patients who survive, the censored group includes patients who are lost to follow-up, who withdraw from the study or who die without the investigators' knowledge. Classifying patients who do not experience the event for whatever reason as 'censored' allows them to be included in the analysis.

Assumptions

The assumptions for using Kaplan–Meier survival analyses are shown in Box 11.1. These analyses are non-parametric tests and thus no assumptions about the distributions of variables need to be met.

Box 11.1 Assumptions for using Kaplan–Meier survival analysis

The assumptions for using Kaplan–Meier survival analysis are that:

- the participants must be independent, that is each participant appears only once in their group
- the groups must be independent, that is each participant is in one group only
- the measurement of time to the event must be precise
- the start point and the event must be clearly defined
- participants' survival prospects remain constant, that is participants enrolled early or late in the study have the same survival prospects
- the probability of censoring is not related to the probability of the event

In survival analyses, it is essential that the time to the event be measured accurately. For this, regular observations need to be conducted rather than, for example, surmising that the event occurred between two routine examinations[2]. When it is only known that an event occurred between two points in time, for example if observations are only taken every 6 months, the data are said to be interval censored[3]. If time to the event is not measured precisely, the survival probabilities will be biased.

Both the start point, that is entry into the study, the inclusion criteria and the event must be well defined to avoid bias in the analyses. This is especially important when using survival analyses to describe the natural history of a condition[4]. Using start points that are prone to bias, such as patient recall of a diagnosis or attendance at a doctor surgery to define the presence of an illness, will result in unreliable survival probabilities.

The reason for the event must also be clearly defined. When an event occurs that is not due to the condition being investigated, careful consideration needs to be given to whether it is treated as an event or as a withdrawal. In clinical trials, combined events for example an event that combines death, acute myocardial infarction or cardiac arrest are often used to test the effectiveness of interventions[5].

In addition, patients who are censored must have the same survival prospects as patients who continue in the study, that is the risk of the event should not be related to the reasons for censoring or loss to follow-up[2]. Thus factors that influence patients' survival prospects, such as different treatment options, should not change over the study period and patients who experience more sickness in one treatment group should not be preferentially lost to follow-up compared with patients who experience less sickness in another treatment group. Secular trends in survival can also occur if patients enrolled early have a different underlying prognosis from those enrolled towards the end of the study. This would bias estimates of risk of survival in a cohort study but is not so important in clinical trials in which randomisation balances important prognostic factors between the groups.

As with all analyses, if the total number of patients in any group is small, say less than 30 participants in each group, the standard errors around the summary statistics will be large and therefore the survival estimates will be imprecise.

When conducting a survival analysis, the data need to be entered with one binary variable indicating whether or not the event occurred and a continuous variable indicating the time to the event or the time to follow-up. The event is usually coded as '1' and censored cases coded as '0', although other coding such as '1' and '2' could be used.

Research question

The file **survival.sav** contains the data from 56 patients enrolled in a trial of two treatments in which 30 patients received the new treatment and 26 patients received the standard treatment. A total of 39 patients died.

Question:	Is the survival rate in the new treatment group higher than in the standard treatment group?
Null hypothesis:	That there is no difference in survival rates between treatment groups.

Variables: Outcome variable = death (binary event)
Explanatory variables = time of follow-up (continuous), treatment group (categorical, two levels)

The commands shown in Box 11.2 can be used to obtain a Kaplan–Meier statistic to assess whether the differences in survival times between the two treatment groups are significantly different.

Box 11.2 SPSS commands to obtain survival curves

SPSS Commands

survival – SPSS Data Editor
    Analyze →Survival→ Kaplan-Meier
Kaplan-Meier
    Highlight days and click into Time
    Highlight event and click into Status
    Click on Define Event
Kaplan-Meier: Define Event for Status Variable
    Type 1 in Single value box, click Continue
Kaplan-Meier
    Highlight Treatment group and click into Factor
    Click Compare Factor
Kaplan-Meier: Compare factor levels
    Under Test Statistics tick Log rank, Breslow, Tarone Ware, click Continue
Kaplan-Meier
    Click Options
Kaplan-Meier: Options
    Under Statistics tick Survival table(s) (default) and tick Mean and median survival (default)
    Under Plots, tick Survival
    Click Continue
Kaplan-Meier
    Click OK

Kaplan–Meier

```
Survival Analysis for DAYS
Factor GROUP = New treatment

Time   Status     Cumulative     Standard    Cumulative     Number
                    Survival       Error       Events      Remaining
 5       0                                       0            29
 7       0                                       0            28
 8       0                                       0            27
 9       1        .9630          .0363           1            26
 9       0                                       1            25
12       1        .9244          .0514           2            24
```

```
15       1        .8859          .0620           3            23
16       1        .8474          .0703           4            22
16       0                                      4            21
16       0                                      4            20
19       0                                      4            19
20       0                                      4            18
23       0                                      4            17
24       0                                      4            16
25       0                                      4            15
29       0                                      4            14
31       0                                      4            13
32       1        .7822          .0902           5            12
32       0                                      5            11
36       1        .7111          .1064           6            10
38       0                                      6             9
40       0                                      6             8
41       0                                      6             7
41       0                                      6             6
42       0                                      6             5
43       0                                      6             4
48       0                                      6             3
49       0                                      6             2
58       0                                      6             1
59       0                                      6             0

 Number of Cases: 30      Censored: 24 (80.00%)   Events: 6

          Survival Time  Standard Error   95% Confidence Interval
 Mean:           49                 4     (41, 56 )(Limited to 59 )

Survival Analysis for DAYS
Factor GROUP = Standard treatment

Time  Status      Cumulative     Standard     Cumulative     Number
                   Survival        Error        Events    Remaining

 1       1                                       1            25
 1       1                                       2            24
 1       1       .8846          .0627             3            23
 2       1       .8462          .0708             4            22
 3       1       .8077          .0773             5            21
 4       1                                       6            20
 4       1       .7308          .0870             7            19
 6       0                                       7            18
 7       1       .6902          .0911             8            17
17       1       .6496          .0944             9            16
20       0                                       9            15
21       1                                      10            14
21       1       .5630          .0997            11            13
31       0                                      11            12
31       0                                      11            11
32       0                                      11            10
33       0                                      11             9
33       0                                      11             8
36       0                                      11             7
```

```
39       0                                       11          6
40       0                                       11          5
40       0                                       11          4
41       0                                       11          3
43       0                                       11          2
50       0                                       11          1
65       0                                       11          0

 Number of Cases:  26       Censored:   15    ( 57.69%)   Events:11
         Survival Time   Standard Error   95% Confidence Interval
 Mean:          40                  6 ( 29, 51 )(Limited to 65 )
```

The Survival Analysis for Days tables show the cumulative survival rate at each follow-up time point which is calculated each time an event occurs. The column labelled 'Time' indicates the day the event occurred. From the Cumulative Survival column, the cumulative survival is 0.7111 at 36 days in group 1 (new treatment) and 0.5630 at 21 days in group 2 (standard treatment). The Kaplan–Meier method produces a single summary statistic of survival time, that is the mean[6]. Mean survival is calculated as the summation of time divided by the number of patients who remain uncensored. The mean survival time shown at the foot of each table is higher in the new treatment group at 49 days than in the standard treatment group at 40 days.

```
Survival Analysis for DAYS
                          Total    Number     Number       Per cent
                                   Events    Censored      Censored
GROUP   New treatment       30       6          24          80.00
GROUP   Standard treatment  26      11          15          57.69
Overall                     56      17          39          69.64
```

The final Survival Analysis for Days table also shows summary statistics of the number in each group, the number of events and the number and per cent censored. These statistics show that there were fewer events but more patients who were censored in the new treatment group.

```
Test Statistics for Equality of Survival Distributions for GROUP
              Statistic        df        Significance
Log Rank           3.27        1            .0705
Breslow            5.32        1            .0211
Tarone-Ware        4.39        1            .0362
```

The Test Statistics for Equality of Survival Distributions table shows the three tests that can be used to test the null hypothesis that there is an equal risk of death in both groups, that is the Log Rank, Breslow and Tarone-Ware tests. These tests are similar to chi-square tests in that the number of observed events is compared with the number of expected events. All three tests have low power for detecting differences when survival curves cross one another.

The Log Rank statistic, which is derived from a whole pattern test in which the entire survival curve is used, is the most commonly reported survival statistic[7]. The Log Rank test is appropriate when the survival curves continue to diverge over time but this test becomes unreliable if one or more groups have small numbers and is not recommended if the survival curves from two groups cross one another.

The Breslow and Tarone-Ware tests are both weighted variants of the Log Rank test because in these tests different weightings are given to particular points of the survival curve[7]. The Breslow test gives greater weight to early observations when the sample size is larger and is less sensitive to later observations when the sample size is smaller. This test is appropriate when there are few ties in the data, that is patients with equal survival times. The Tarone-Ware test provides a compromise between the Log Rank and the Breslow tests but is rarely used.

The SPSS output shows how the three tests can lead to different conclusions about whether there is a significant difference in the survival rate between groups. The Log Rank test is not significant at $P = 0.0705$. However, this test is not appropriate in this situation in which the number of patients remaining after 33 to 36 days is small with less than 10 patients in each group.

The Breslow test is significant at $P = 0.0211$ and is the most appropriate test to report here because more weight is placed on earlier observations when group sizes are larger. In this example, the Breslow P value is more significant than the Log Rank P value because more weight has been placed on the early observations when survival rates between the groups are different than on later observations when survival rates between the groups are more similar as shown in the Survival Functions plot in the next section. If early observations were more similar between groups and later observations more different, the Log Rank P value would have been more significant than the Breslow P value.

Reporting the results

When reporting data from survival analyses, the P values from the statistical analyses do not convey information about the size of the effect. In addition to P values, summary statistics such as the follow-up time of each group, the total number of events and the number of patients who remain event free are important for interpreting the data. This information can be reported as shown in Table 11.1.

Table 11.1 Survival characteristics of study sample

Group	Number of cases	Number of events	Number censored	Mean survival time in days (95% CI)
New treatment	30	6	24 (80.0%)	49 (41, 56)
Standard treatment	26	11	15 (57.7%)	40 (29, 51)

Survival plots

Survival plots, which are called Kaplan–Meier curves, are widely used with 40% of publications from randomised controlled trials including a survival plot[5]. In plotting Kaplan–Meier curves, the data are first ranked in ascending order according to time. A curve is then plotted for each group by calculating the proportion of patients who remain in the study and who are censored each time an event occurs. Thus, the curves do not change at the time of censoring but only when the next event occurs.

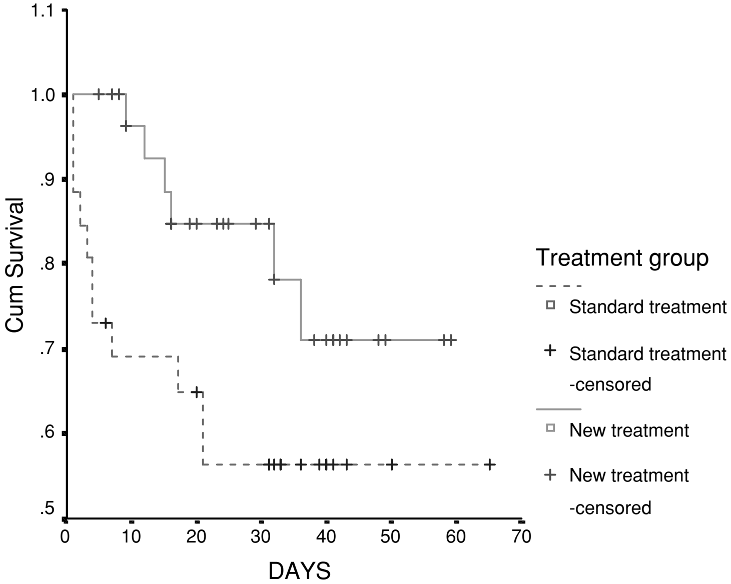

Figure 11.1 Plot showing survival functions of treatment group.

The survival plot shows the proportion of patients who are free of the event at each time point. The steps in the curves occur each time an event occurs and the bars on the curves indicate the times at which patients are censored. The plots show the survival time for a typical patient. In the survival plot shown in Figure 11.1 the standard treatment group, which is the lower curve, has a poorer survival time than the new treatment group, which is the upper curve. The sections of the curves where the slope is steep, in this case the earlier parts, indicate the periods when patients are most at risk for experiencing the event. It is always advisable to plot survival curves before conducting the tests of significance.

Plotting survival curves

There are several ways to plot survival curves and the debate about whether they should go up or down and how the *y*-axis should be scaled continues[5].

In SPSS, different presentations of the survival curve can be obtained in the *Plot → Options* commands.

Plotting survival curves is not problematic when the study sample is large and the follow-up time is short. However, when the number of patients who remain at the end is small, survival estimates are poor. Thus, it is important to end plots when the number in follow-up has not become too small. In the above example, the curves should be truncated to 31 days when the number in each group is 10 or more and should not be continued to 65 days when all patients in the standard treatment group have experienced the event or are censored.

The scaling of the *y*-axis is important because differences between groups can be visually magnified or reduced by shortening or lengthening the axis. In practice, a scale only slightly larger than the event rate is generally recommended to provide visual discrimination between groups rather than the full scale of 0 to 1.[5] However, this can tend to make the differences between the curves seem larger than they actually are, as in the SPSS plot in which the *y*-axis scale ranges from 0.5 to 1.0.

Questions for critical appraisal

The questions that should be asked when critically appraising a journal article that reports a survival analysis are shown in Box 11.3.

Box 11.3 Questions to ask when critically appraising the literature

The following questions can be asked when critically appraising the literature:

- Is the start point and event clearly defined and free of recall or other bias?
- Has time been measured accurately?
- Have any factors preferentially changed the patient's survival prospects over the course of the study?
- Is a figure reported appropriately?
- Is the sample size in each group sufficient?

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Glossary

Adjusted *R* square *R* square is the coefficient of determination that is adjusted for the number of explanatory variables included in the regression model. This value can be used to compare regression models that have a different number of explanatory variables.

Asymptotic methods Commonly used statistical tests based on assumptions that the sample size is large and the data are normally distributed or, if the data are categorical, that the condition of interest occurs frequently, say in more than 5% of the sample.

Balanced design Studies with a balanced design have an equal number of observations in each cell. This can only be achieved in experimental studies or by data selection. Most observational studies have an unbalanced design with unequal number of observations in the cells.

Bivariate tests Tests in which the relation between two variables is estimated, for example an outcome and an explanatory variable.

Case–control study A study design in which individuals with the disease of interest (cases) are selected and compared to a control or reference group of individuals without the disease.

Censoring A term used to indicate that an event did not occur in a survival analysis. The reasons for censoring could be that the participant withdrew, was lost to follow-up or did not experience the event.

Chi-square A statistic used to test whether the frequency of an outcome in two or more groups is significantly different, or that the rows and columns of a crosstabulation table are independent.

Collinearity A term used when two variables are strongly related to one another. Collinearity between explanatory variables inflates the standard errors and causes imprecision because the variation is shared. Thus, the model becomes unstable (i.e. unreliable).

Complete design A study design is complete when there are one or more observations in each cell and is incomplete when some cells are empty.

Confidence interval The 95% confidence interval is the interval in which there is 95% certainty that the true population value lies. Confidence intervals are calculated around summary statistics such as mean values or proportions. For samples with more than 30 cases, a 95% confidence is calculated as the summary statistic ± (SE × 1.96), where SE equals standard error. The confidence limits are the values at the ends of the confidence interval.

Confounder Confounders are nuisance variables that are related to the outcome and to the explanatory variables and whose effect needs to be minimised in the study design or analyses so that the results are not biased.

Cook's distances Measure of influence used in multivariate models. Values greater than $4/(n - k - 1)$ are considered influential (n = sample size, k = number of variables in model).

Discrepancy A measure of how much a case is in line with other cases in a multivariate model.

Dummy variables A series of binary variables that have been derived from a multi-level ordinal variable.

Effect size The distance between two mean values described in units of their standard deviations.

Error term See Residual.

Eta squared A measure of the strength of association between the outcome and the explanatory factors. As such, eta^2 is an approximation to R squared.

Exact statistics Statistics calculated using exact factorial or binomial methods rather than asymptotic methods. Exact statistics are used when the numbers in a cell or group are small and the assumptions for asymptotic statistical tests are violated.

Explanatory variable A variable that is a measured characteristic or an exposure and that is hypothesised to influence an event or a disease status (i.e. outcome variable). In cross-sectional and cohort studies, explanatory variables are often exposure variables.

***F* value** An F value is a ratio of variances. For one-way ANOVA, F is the between-group MS/within MS where MS equals mean sum of squares. For factorial ANOVA, F is the MS for factor/residual MS. For regression, F is the MS regression/residual MS.

Factorial ANOVA A factorial ANOVA is used to examine the effects of two or more factors, or explanatory variables, on a single outcome variable. When there are two explanatory factors, the model is described as a two-way ANOVA, when there are three factors as a three-way ANOVA, etc.

Heteroscedasticity Heteroscedasticity indicates that the variances in cells in a multivariate model are unequal or the variance across a model is not constant.

Homoscedasticity Homoscedasticity indicates that the variances in cells in a multivariate model are not different or that there is constant variance over the length of a model.

Incidence Rate of new cases in a random population sample in a specified time, for example, 1 year.

Influence Influence is calculated as leverage multiplied by discrepancy and is used to assess the change in a regression coefficient when a case is deleted.

Inter-quartile range A measure of spread that is the width of the band that contains the middle half of the data that lies between the 25th and 75th percentiles.

Interval scale variable A variable with values where differences in intervals or points along the scale can be made e.g. the difference between 5 and 10 is the same as the difference between 85 and 90.

Intervening variable A variable that acts on the pathway between an outcome and an exposure variable.

Kurtosis A measure of whether the distribution of a variable is peaked or flat. Measures of kurtosis between –1 and 1 indicate that the distribution has an approximately normal bell shape curve and values around –2 to +2 are a warning of some degree of kurtosis. Values below –3 or above +3 indicate that there is significant peakedness or flatness and therefore that the data are not normally distributed.

Leverage A measure of the influence of a point on the fit of a regression. Leverage can range from 0 (no influence) to $n - 1/n$ where n equals the sample size. Leverage values close to 1 indicate total influence.

Likelihood ratio A statistic used to combine sensitivity and specificity into a single estimate that indicates how a positive test result will change the odds that a patient has the disease.

Linear-by-linear association A statistic used to test whether a binary outcome increases or decreases over an ordered categorical exposure variable. Although this is printed by SPSS when chi-square is requested, the trend is computed using a Pearson correlation coefficient.

Mahalanobis distance This is the distance between a case and the centroid of the remaining cases, where the centroid is the point where the means of the explanatory variables intersect. Mahalanobis distance is used to identify multivariate outliers in regression analyses. A case with a Mahalanobis distance above the chi-squared critical value at $P < 0.001$ with degrees of freedom equal to the number of explanatory variables in the model is a multivariate outlier.

Maximum value The largest numerical value of a variable.

Mean A measure of the centre or the average value of the data.

Mean square A term used to describe variance in a regression model. This term is the sum of the squares divided by their degrees of freedom.

Median The point at which half the measurements lie above and below this value, that is the point that marks the centre of the data.

Minimum value The smallest numerical value of a variable.

Multivariate tests Tests with more than one explanatory variable in the model.

Negative predictive value The proportion of individuals who have a negative diagnostic test result and who do not have the disease.

Nominal variable A variable with values that do not have any ordering or meaningful ranking and are generally categories e.g. values to indicate retired, employed or unemployed.

Normal score See z score.

Null hypothesis A null hypothesis states that there is no difference between the means of the populations from which the samples were drawn, that is population means are equal or that there is no relationship between two or more variables. If the null hypothesis is accepted, this does not necessarily mean that the null hypothesis is true but can suggest that there is not sufficient or strong enough evidence to reject it.

Odds ratio An estimate of risk of disease given exposure, or vice versa, that can be calculated from any type of study design.

One-tailed tests When the direction of the effect is specified by the alternate hypothesis e.g. $\mu > 50$ a one-tailed test is used. The tail refers to the end of the probability curve. The critical region for a one sided test is located in only one tail of the probability distribution. One-tailed tests are more powerful than two-tailed tests for showing a significant difference because the critical value for significance is lower and are rarely used in health care research.

Ordinal variable A variable with values that indicate a logical order such as codes to indicate socioeconomic or educational status.

Outcome variable The outcome of interest in a study, that is the variable that is dependent on or is influenced by other variables (explanatory variables) such as exposures, risk factors, etc.

Outliers There are two types of outliers: univariate and multivariate. Univariate outliers are defined as data points that have an absolute z score greater than 3. This term is used to describe values that are at the extremities of the range of data points or are separated from the normal range of the data. For small sample sizes, data points that have an absolute z score greater than 2.5 are considered to be univariate outliers. Multivariate outliers are data values that have an extreme value on a combination of explanatory variables and exert too much leverage and/or discrepancy.

***P* value** A P value is the probability of a test statistic occurring if the null hypothesis is true. P values that are large are consistent with the null hypothesis. On the other hand, P values that are small, say less than 0.05, lead to rejection of the null hypothesis because there is a small probability that the null hypothesis is true. P values are also called significance levels. In SPSS output, P value columns are often labelled 'Sig.'

Partial correlation The correlation between two variables after the effects of a third or confounding variable have been removed.

Population A collection of individuals to whom the researcher is interested in making an inference, for example all people residing in a specific region or in an entire country, or all people with a specific disease.

Positive predictive value The proportion of individuals with a positive diagnostic test result who have the disease.

Power The ability of the study to demonstrate an effect or association if one exists, that is to avoid type II errors. Power can be influenced by many factors including the frequency of the outcome, the size of the effect, the sample size and the statistical tests used.

Prevalence Rate of total cases in a random population sample in a specified time, for example 1 year.

Quartiles Obtained by placing observations in an increasing order and then dividing into four groups so that 25% of the observations are in each group.

The cut-off points are called quartiles. The four groups formed by the three quartiles are called 'fourths' or 'quarters'

Quintiles Obtained by placing observations in an increasing order and then dividing into five groups so that 20% of the observations are in each group. The cut-off points are called quintiles.

***R* square** The *R* square value (coefficient of determination) is the squared multiple correlation coefficient and indicates the per cent of the variance in the outcome variable that can be explained or accounted for by the explanatory variables.

***r* value** Pearson's correlation coefficient that measures the linear relationship between two continuous normally distributed variables.

R Multiple correlation coefficient that is the correlation between the observed and predicted values of the outcome variable.

Range The difference between the lowest and the highest numerical values of a variable, that is the maximum value subtracted from the minimum value. The term range is also often used to describe the values that are the limits of the range, that is the minimum and the maximum values e.g. range 0 to 100.

Ratio scale variable An interval scale variable with a true zero value so that the ratio between two values on the scale can be calculated, e.g. age in years is a ratio scale variable but calendar year of birth is not.

Relative risk The risk of disease given exposure divided by the risk of disease given no exposure, which can only be calculated directly from a random population sample. In case–control studies, relative risk is estimated by an odds ratio.

Residual The difference between a participant's value and the predicted value, or mean value, for the group. This term is often called the error term.

Risk The probability that any individual will develop a disease. Risk is calculated as the number of individuals who have the disease divided by the total number of individuals in the sample or population.

Risk factor An aspect of behaviour or lifestyle or an environmental exposure that is associated with a health related condition.

Sample Selected and representative part of a population that is used to make inferences about the total population from which it is drawn.

Sensitivity Proportion of disease positive individuals who are correctly diagnosed by a positive diagnostic test result.

Significance level See *P* value.

Skewness A measure of whether the distribution of a variable has a tail to the left or right hand side. Skewness values between –1 and +1 indicate slight skewness and values around –2 and +2 are a warning of a reasonable degree of skewness but possibly still acceptable. Values below –3 or above +3 indicate that there is significant skewness and that the data are not normally distributed.

Specificity The proportion of disease negative individuals who are correctly identified as disease free by a negative diagnostic test result.

Standard deviation A measure of spread such that it is expected that 95% of the measurements lie within 1.96 standard deviations above and below the mean. This value is the square root of the variance.

Standardised coefficients Partial regression coefficients that indicate the relative importance of each variable in the regression equation. These coefficients are in standardised units similar to *z* scores and their dimension allows them to be compared with one another.

Standard error A measure of precision that is the size of the error around a mean value or proportion, etc. For continuous variables, the standard error around a mean value is calculated $\mathrm{SD}/\sqrt{n}$. For other statistics such as proportions and regression estimates, different formulae are used. For all statistics, the SE will become smaller as the sample size increases for data with the same spread or characteristics.

SE of the estimate This is the approximate standard deviation of the residuals around a regression line. This statistic is a measure of the variation that is not accounted for by the regression line. In general, the better the fit, the smaller the standard error of the estimate.

String variable A variable that generally consists of words or characters but may include some numbers. This type of variable is also known as an alphanumeric variable.

***t*-value** A *t*-distribution is closely related to a normal distribution but depends on the number of cases in a sample. A *t*-value, which is calculated by dividing a mean value by its standard error, gives a number from which the probability of an event occurring is estimated from a *t*-table.

Trimmed mean The 5% trimmed mean is the mean calculated after 5% of the data (i.e. outliers) are removed. This method is sometimes used in sports competitions, for example skating, when several judges rate performance on a scale.

Two-tailed tests When the direction of the effect is not specified by the alternate hypothesis e.g. $\mu \neq 50$ a two-tailed test is used. The tail refers to the end of the probability curve. The critical region for a two sided test is located in both tails of the probability distribution. Two-tailed tests are used in most research studies.

Type I error A term used when a statistically significant difference between two study groups is found although the null hypothesis is true. Thus, the null hypothesis is rejected in error.

Type II error A term used when a clinically important difference between two study groups does not reach statistical significance. Thus, the null hypothesis is not rejected when it is false. Type II errors typically occur when the sample size is small.

Type sum of squares (SS) Type III SS are used in ANOVA for unbalanced study designs when all cells have equal importance but no cells are empty. This is the most common type of study design in health research. Type I SS are used when all cell numbers are equal, type II is used when some cells have equal importance and type IV is used when some cells are empty.

Univariate tests Descriptive tests in which the distribution or summary statistics for only one variable are reported.

Unstandardised coefficients These are the regression estimates such as y and x in the equation $y = a + bx$ where 'a' is the constant and 'b' is the coefficient for explanatory variable.

Variance A measure of spread that is calculated from the sum of the deviations from the mean, which have been squared to remove negative values.

***Z* score** This is the number of standard deviations of a value from the mean. Z scores, which are also known as normal scores, have a mean of zero and a standard deviation of one unit. Values can be converted to z scores for variables with a normal or non-normal distribution; however, conversion to z scores does not transform the shape of the distribution.

Useful Web sites

A New View of Statistics

http://www.sportsci.org/resource/stats/index.html

A peer-reviewed website that includes comprehensive explanations and discussion of many statistical techniques including confidence intervals, chi-squared and ANOVA, plus some Excel spreadsheets to calculate summary statistics that are not available from commonly used statistical packages.

Diagnostic test calculator

http://araw.mede.uic.edu/cgi-alansz/testcalc.pl

Online program for calculating statistics related to diagnostic tests such as sensitivity, specificity and likelihood ratio.

Epi Info

http://www.cdc.gov/epiinfo/downloads.htm

With Epi Info, a questionnaire or form can be developed, the data entry process can be customised and data can be entered and analysed. Epidemiologic statistics, tables, graphs, maps, and sample size calculations confidence intervals around a proportion can be produced. Epi Info can be downloaded free.

Graphpad Quickcalcs Free Online calculators for scientists

http://www.graphpad.com/quickcalcs/index.cfm

Online program for calculating many statistical tests from summary data including McNemars, NNT, etc.

HyperStat Online Textbook

http://davidmlane.com/hyperstat/

Provides information on a variety of statistical procedures, with links to other related Web sites, recommended books and statistician jokes.

Martin Bland Web page

http://www.mbland.sghms.ac.uk

Web page with links to talks on agreement, cluster designs, etc. and statistics advice and access to free statistical software. Also includes an index to all BMJ statistical notes that are online.

Multivariate Statistics: Concepts, Models and Applications

http://www.psychstat.smsu.edu/multibook2/mlt.htm

A Web site that includes graphs to illustrate multivariate concepts and detailed examples of multiple regression, two-way ANOVA and other multivariate tests. Includes examples of how to interpret SPSS output.

PA 765 Statnotes: An Online Textbook by G David Garson

http://www2.chass.ncsu.edu/garson/pa765/statnote.htm

Notes on a range of statistical tests including *t*-tests, chi-squared, ANOVA, ANCOVA, correlations, regression and logistic regression are presented in detail. Also, assumptions for each statistical test, definition of terms and links to other statistical Web sites are given.

Public Health Archives

http://www.jiscmail.ac.uk/archives/public-health.html

Mailbase to search for information or post queries about statistics, study design issues, etc. This site also has details of international courses, etc.

Raynald's SPSS Tools

http://pages.infinit.net/rlevesqu/index.htm

Web site with syntax, macros and online tutorials on how to use SPSS and with links to other statistical Web sites.

Russ Lenth's power and sample size page

http://www.stat.uiowa.edu/~rlenth/Power/

A graphical interface for studying the power of one or more tests including the comparison of two proportions, *t*-tests and balanced ANOVA.

Simple Interactive Statistical Analysis (SISA)

http://home.clara.net/sisa

Simple interactive program that provides tables to conduct statistical analysis such as chi-square and *t* tests from summary data.

Statistics on the Web

http://www.execpc.com/~helberg/statistics.html

Links to statistics resources including online education courses, statistics books and programs and professional organisations.

StatPages.net

http://members.aol.com/johnp71/javastat.html

A conveniently accessible statistical software package with links to online statistics books, tutorials, downloadable software, and related resources.

StatSoft – Electronic Statistics Textbook

http://www.statsoft.com/textbook/stathome.html

Provides an overview of elementary concepts and continues with a more in-depth exploration of specific areas of statistics including ANOVA, regression and survival analysis. A glossary of statistical terms and a list of references for further study are included.

Stat/Transfer

http://www.stattransfer.com.

Stat/Transfer is designed to simplify the transfer of statistical data between different programs. Stat/Transfer automatically reads statistical data in the internal format of one of the supported programs such as Microsoft Access, FoxPro, Minitab, SAS and Epi Info and will then transfer as much of the information as is present and appropriate to the internal format of another.

UCLA Academic Technology Services

http://www.ats.ucla.edu/stat/spss/

Helpful Web site with online SPSS textbook and examples and frequently asked questions, with detailed information about regression and ANOVA.

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