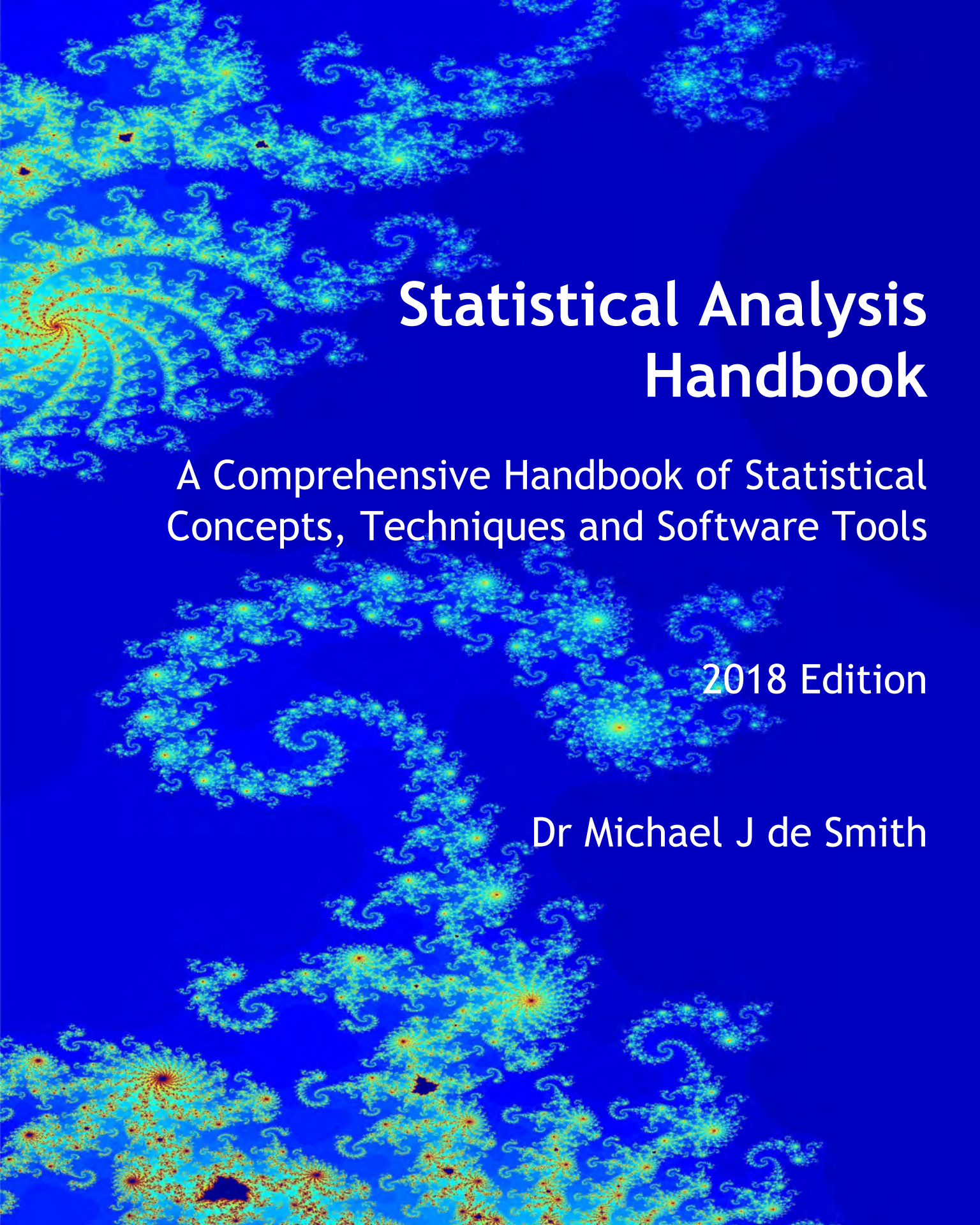

Statistical Analysis Handbook

A Comprehensive Handbook of Statistical Concepts, Techniques and Software Tools

2018 Edition

Dr Michael J de Smith

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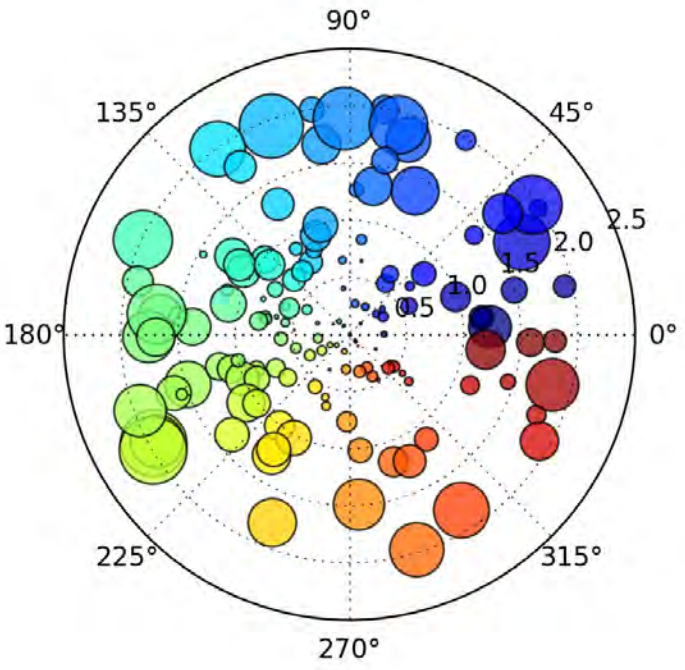

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Front inside cover image: Polar bubble plot (MatPlotLib, Python)

Rear inside cover image: Florence Nightingale's polar diagram of causes of mortality, by month (source: Wikipedia)

Cover image: Mandlebrot set fractal

Table of Contents

Chapter 1

1 Introduction

The definition of what is meant by *statistics* and *statistical analysis* has changed considerably over the last few decades. Here are two contrasting definitions of what statistics is, from eminent professors in the field, some 60+ years apart:

> *"Statistics is the branch of scientific method which deals with the data obtained by counting or measuring the properties of populations of natural phenomena. In this definition 'natural phenomena' includes all the happenings of the external world, whether human or not." Professor Maurice Kendall, 1943, p2* [MK1]

> *"Statistics is: the fun of finding patterns in data; the pleasure of making discoveries; the import of deep philosophical questions; the power to shed light on important decisions, and the ability to guide decisions..... in business, science, government, medicine, industry..." Professor David Hand* [DH1]

As these two definitions indicate, the discipline of statistics has moved from being grounded firmly in the world of measurement and scientific analysis into the world of exploration, comprehension and decision-making. At the same time its usage has grown enormously, expanding from a relatively small set of specific application areas (such as design of experiments and computation of life insurance premiums) to almost every walk of life. A particular feature of this change is the massive expansion in information (and misinformation) available to all sectors and age-groups in society. Understanding this information, and making well-informed decisions on the basis of such understanding, is the primary function of modern statistical methods.

Our objective in producing this Handbook is to be comprehensive in terms of concepts and techniques (but not necessarily exhaustive), representative and independent in terms of software tools, and above all practical in terms of application and implementation. However, we believe that it is no longer appropriate to think of a standard, discipline-specific textbook as capable of satisfying every kind of new user need. Accordingly, an innovative feature of our approach here is the range of formats and channels through which we disseminate the material — web, ebook and print. A major advantage of the electronic formats is that the text can be embedded with internal and external hyperlinks (shown underlined). In this Handbook we utilize both forms of link, with external links often referring to a small number of well-established sources, including MacTutor for bibliographic information and a number of other web resources, such as Eric Weisstein's Mathworld and the statistics portal of Wikipedia, that provide additional material on selected topics.

The treatment of topics in this Handbook is relatively informal, in that we do not provide mathematical proofs for much of the material discussed. However, where it is felt particularly useful to clarify how an expression arises, we do provide simple derivations. More generally we adopt the approach of using descriptive explanations and worked examples in order to clarify the usage of different measures and procedures. Frequently convenient software tools are used for this purpose, notably SPSS/PASW, The R Project, MATLab and a number of more specialized software tools where appropriate.

Just as all datasets and software packages contain errors, known and unknown, so too do all books and websites, and we expect that there will be errors despite our best efforts to remove these! Some may be genuine errors or misprints, whilst others may reflect our use of specific versions of software packages and their documentation. Inevitably with respect to the latter, new versions of the packages that we have used to illustrate this Handbook will have appeared even before publication, so specific examples, illustrations and comments on scope or restrictions may have been superseded. In all cases the user should review the documentation provided with the

software version they plan to use, check release notes for changes and known bugs, and look at any relevant online services (e.g. user/developer forums and blogs on the web) for additional materials and insights.

The interactive web and PDF versions of this Handbook provide color images and active hyperlinks, and may be accessed via the associated Internet site: www.statsref.com. The contents and sample sections of the PDF version may also be accessed from this site. In both cases the information is regularly updated. The Internet is now well established as society's principal mode of information exchange, and most aspiring users of statistical methods are accustomed to searching for material that can easily be customized to specific needs. Our objective for such users is to provide an independent, reliable and authoritative first port of call for conceptual, technical, software and applications material that addresses the panoply of new user requirements.

Readers wishing to obtain a more in-depth understanding of the background to many of the topics covered in this Handbook should review the Suggested Reading topic.

References

[DH1] D Hand (2009) President of the Royal Statistical Society (RSS), RSS Conference Presentation, November 2009

[MK1] Kendall M G, Stuart A (1943) The Advanced Theory of Statistics: Volume 1, Distribution Theory. Charles Griffin & Company, London. First published in 1943, revised in 1958 with Stuart

1.1 How to use this Handbook

This Handbook is designed to provide a wide-ranging and comprehensive, though not exhaustive, coverage of statistical concepts and methods. Unlike a Wiki the Handbook has a more linear flow structure, and in principle can be read from start to finish. In practice many of the topics, particularly some of those described in later parts of the document, will be of interest only to specific users at particular times, but are provided for completeness. Users are recommended to read the initial four topics — Introduction, Statistical Concepts, Statistical Data and Descriptive Statistics, and then select subsequent sections as required.

Navigating around the PDF or web versions of this Handbook is straightforward, but to assist this process a number of special facilities have been built into the design to make the process even easier. These facilities include:

- Tests Index — this is a form of 'how to' index, i.e. it does not assume that the reader knows the name of the test they may need to use, but can navigate to the correct item by the index description
- Reference links and bibliography — within the text all books and articles referenced are linked to the full reference at the end of the topic section (in the References subsection) in the format [XXXn] and in the complete bibliography at the end of the Handbook
- Hyperlinks — within the document there are two types of hyperlink: (i) internal hyperlinks — when clicking on these links you will be directed to the linked topic within this Handbook; (ii) external hyperlinks — these provide access to external resources for which you need an active internet connection. When the external links are clicked the appropriate topic is opened on an external website such as Wikipedia
- Search facilities — the web and PDF versions of this Handbook facilitate free text search, so as long as you know roughly what you are looking for, you should be able to find it using this facility

1.2 Intended audience and scope

Ian Diamond, Statistician and at the time Chief Executive of the UK's Economic and Social Research Council (ESRC), gave the following anecdote (which I paraphrase) during a meeting in 2009 at the Royal Statistical Society in London: "Some time ago I received a brief email from a former student. In it he said

> *'your statistics course was the one I hated most at University and was more than glad when it was over.... but in my working career it has been the most valuable of any of the courses I took... !'"*

So, despite its challenges and controversies, taking time to get to grips with statistical concepts and techniques is well worth the effort.

With this perspective in mind, this Handbook has been designed to be accessible to a wide range of readers — from undergraduates and postgraduates studying statistics and statistical analysis as a component of their specific discipline (e.g. social sciences, earth sciences, life sciences, engineers), to practitioners and professional research scientists. However, it is not intended to be a guide for mathematicians, advanced students studying statistics or for professional statisticians. For students studying for academic or professional qualifications in statistics, the level and content adopted is that of the Ordinary and Higher Level Certificates of the Royal Statistical Society (RSS), offered until 2017. Much of the material included in this Handbook is also appropriate for the Graduate Diploma level also, although we have not sought to be rigorous or excessively formal in our treatment of individual statistical topics, preferring to provide less formal explanations and examples that are more approachable by the non-mathematician with links and references to detailed source materials for those interested in derivation of the expressions provided.

The Handbook is much more than a cookbook of formulas, algorithms and techniques. Its aim is to provide an explanation of the key techniques and formulas of statistical analysis, often using examples from widely available software packages. It stops well short, however, of attempting a systematic evaluation of competing software products. A substantial range of application examples is provided, but any specific selection inevitably illustrates only a small subset of the huge range of facilities available. Wherever possible, examples have been drawn from non-academic and readily reproducible sources, highlighting the widespread understanding and importance of statistics in every part of society, including the commercial and government sectors.

References

Royal Statistical Society: Professional Development section:
https://www.rss.org.uk/RSS/pro_dev/RSS/pro_dev/Professional_Development.aspx

1.3 Suggested reading

There are a vast number of books on statistics — Amazon alone lists 10,000+ "professional and technical" works with *statistics* in their title. There is no single book or website on statistics that meets the need of all levels and requirements of readers, so the answer for many people starting out will be to acquire the main 'set books' recommended by their course tutors and then to supplement these with works that are specific to their application area. Every topic and subtopic in this Handbook almost certainly has at least one entire book devoted to it, so of necessity the material we cover can only provide the essential details and a starting point for deeper understanding of each topic. As far as possible we provide links to articles, web sites, books and software resources to enable the reader to pursue such questions as and when they wish.

Most statistics texts do not make for easy or enjoyable reading! In general they address difficult technical and philosophical issues, and many are demanding in terms of their mathematics. Others are much more approachable — these books include 'classic' undergraduate text books such as Feller (1950, [FEL1]), Mood and Graybill (1950, [MOO1]), Hoel (1947, [HOE1]), Adler and Roessler (1960, [ADL1]), Brunk (1960, [BRU1]), Snedecor and Cochrane (1937, [SNE1]) and Yule and Kendall (1950, [YUL1]) — the dates cited in each case are when the books were originally published; in most cases these works then ran into many subsequent editions and though most are now out-of-print some are still available. A more recent work, available from the American Mathematical Society and also as a free PDF, is Grinstead and Snell's (1997) An Introduction to Probability [GRI1]. Still in print, and of continuing relevance today, is Huff (1954, [HUF1]) "How to Lie with Statistics" which must be the top selling statistics book of all time. A more recent book, with a similar focus, is Blastland and Dilnot's "The Tiger that Isn't" [BLA1], which is full of examples of modern-day use and misuse of statistics. Another delightful, lighter weight book that remains very popular, is Gonik and Smith's "Cartoon Guide to Statistics" (one of a series of such cartoon guides by Gonik and co-authors, [GON1]). A very useful quick guide is the foldable free PDF format leaflet "Probability & Statistics, Facts and Formulae" published by the UK Maths, Stats and OR Network [UKM1]. The free Statistics Guide for Lawyers (PDF) available on the RSS website is a highly recommended resource (RSS and ICCA) for both lawyers and non-lawyers alike.

Essential reading for anyone planning to use the free and remarkable "R Project" statistical resource is Crawley's "The R Book" (2007, 2015 [CRA1]) and associated data files; and for students undertaking an initial course in statistics using SPSS, Andy Field's "Discovering Statistics Using SPSS" provides a gentle introduction with many worked examples and illustrations [FIE1]. Both Field and Crawley's books are large — around 900 pages in each case. Data obtained in the social and behavioral sciences do not generally conform to the strict requirements of traditional (parametric) inferential statistics and often require the use of methods that relax these requirements. These so-called nonparametric methods are described in detail in Siegel and Castellan's widely used text "Nonparametric Statistics for the Behavioral Sciences" (1998, [SIE1]) and Conover's "Practical Nonparametric Statistics" (1999, [CON1]).

A key aspect of any statistical investigation is the use of graphics and visualization tools, and although technology is changing this field Tufte's "The Visual Display of Quantitative Information" [TUF1] should be considered as essential reading, despite its origins in the 1980s and the dramatic changes to visualization possibilities since its publication.

With a more practical, applications focus, readers might wish to look at classics such as Box *et al*. (1978, 2005, [BOX1]) "Statistics for Experimenters" (highly recommended, particularly for those involved in industrial processes), Sokal and Rohlf (1995, [SOK1]) on Biometrics, and the now rather dated book on Industrial Production

edited by Davies (1961, [DAV1]) and partly written by the extraordinary George Box whilst a postgraduate student at University College London. Box went on to a highly distinguished career in statistics, particular in industrial applications, and is the originator of many statistical techniques and author of several groundbreaking books. He not only met and worked with R A Fisher but later married one of Fisher's daughters! Crow *et al*. (1960, reprinted in 2003, [CRO1]) published a concise but exceptionally clear "Statistics Manual" designed for use by the US Navy, with most of its examples relating to ordnance — it provides a very useful and compact guide for non-statisticians working in a broad range of scientific and engineering fields.

Taking a further step towards more demanding texts, appropriate for mathematics and statistics graduates and post-graduates, we would recommend Kendall's Library of Statistics [KEN1], a multi-volume authoritative series each volume of which goes into great detail on the area of statistics it focuses upon. For information on statistical distributions we have drawn on a variety of sources, notably the excellent series of books by Johnson and Kotz [JON1], [JON2] originally published in 1969/70. The latter authors are also responsible for the comprehensive but extremely expensive nine volume "Encyclopedia of Statistical Sciences" (1998, 2006, [KOT1]). A much more compact book of this type, with very brief but clear descriptions of around 500 topics, is the "Concise Encyclopedia of Statistics" by Dodge (2002, [DOD1]).

With the rise of the Internet, web resources on statistical matters abound. However, it was the lack of a single, coherent and comprehensive Internet resource that was a major stimulus to the current project. The present author's book/ebook/website www.spatialanalysisonline.com has been extremely successful in providing information on Geospatial Analysis to a global audience, but its focus on 2- and 3-dimensional spatial problems limits its coverage of statistical topics. However, a significant percentage of Internet search requests that lead users to this site involve queries about statistical concepts and techniques, suggesting a broader need for such information in a suitable range of formats, which is what this Handbook attempts to provide.

A number of notable web-based resources providing information on statistical methods and formulas should be mentioned. The first is Eric Weisstein's excellent Mathworld site, which has a large technical section on probability and statistics. Secondly there is Wikipedia (Statistics section) — this is a fantastic resource, but is almost by definition not always consistent or entirely independent. This is particularly noticeable for topics whose principal or original authorship reflects the individual's area of specialism: social science, physics, biological sciences, mathematics, economics etc, and in some instances their commercial background (e.g. for specific software packages). Both Mathworld and Wikipedia provide a topic-by-topic structure, with little or no overall guide or flow to direct users through the maze of topics, techniques and tools, although Wikipedia's core structure is very well defined. This contrasts with the last two of our recommended websites: the NIST/SEMATECH online Engineering Statistics e-Handbook, and the UCLA Statistics Online Computational Resource (SOCR). These latter resources are much closer to our Handbook concept, providing information and guidance on a broad range of topics in a lucid, structured and discursive manner. These sites have a further commonality with our project — their use of particular software tools to illustrate many of the techniques and visualizations discussed. In the case of NIST/SEMATECH e-Handbook a single software tool is used, Dataplot, which is a fairly basic, free, cross-platform tool developed and maintained by the NIST. The UCLA Statistics Online Computational Resource project makes extensive use of interactive Java applets to deliver web-enabled statistical tools. The present Handbook references a wider range of software tools to illustrate its materials, including Dataplot, R, SPSS, Excel and XLStat, MATLab, Minitab, SAS/STAT and many others. This enables us to provide a broader ranging commentary on the toolsets available, and to compare the facilities and algorithms applied by the different implementations. Throughout this Handbook we make extensive reference to functions and examples available in R, MATLab and SPSS in particular.

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[TUF1] Tufte E R (2001) The Visual Display of Quantitative Information. 2nd edition. Graphics Press, Cheshire, Conn.

[UKM1] UK Maths, Stats & OR Network. Guides to Statistical Information: Probability and statistics Facts and Formulae. http://icse.xyz/mathstore/index.html

22 Suggested reading

[YUL1] Yule G U, Kendall M G (1950) An Introduction to the Theory of Statistics. Griffin, London, 14th edition (first edition was published in 1911 under the sole authorship of Yule)

Web sites:

Mathworld: http://mathworld.wolfram.com/

NIST/SEMATECH e-Handbook of Statistical Methods: http://www.itl.nist.gov/div898/handbook/

UCLA Statistics Online Computational Resource (SOCR) : http://socr.ucla.edu/SOCR.html

Wikipedia: http://en.wikipedia.org/wiki/Statistics

1.4 Notation and symbology

In order to clarify the expressions used here and elsewhere in the text, we use the notation shown in the table below. Italics are used within the text and formulas to denote variables and parameters. Typically in statistical literature, the Roman alphabet is used to denote sample variables and sample statistics, whilst Greek letters are used to denote population measures and parameters. An excellent and more broad-ranging set of mathematical and statistical notation is provided on the Wikipedia site.

Notation used in this Handbook

Item	Description
$[a,b]$	A closed interval of the Real line, for example [0,1] means the infinite set of all values between 0 and 1, including 0 and 1
(a,b)	An open interval of the Real line, for example (0,1) means the infinite set of all values between 0 and 1, NOT including 0 and 1. This should not be confused with the notation for coordinate pairs, (x,y), or its use within bivariate functions such as $f(x,y)$ — the meaning should be clear from the context
$\{x_i\}$	A set of n values $x_1, x_2, x_3, \ldots x_n$, typically continuous interval- or ratio-scaled variables in the range $(-\infty,\infty)$ or $[0,\infty)$. The values may represent measurements or attributes of distinct objects, or values that represent a collection of objects (for example the population of a census tract)
$\{X_i\}$	An ordered set of n values $X_1, X_2, X_3, \ldots X_n$, such that $X_i \leq X_i+1$ for all i
$\mathbf{X},\mathbf{x}$	The use of bold symbols in expressions indicates matrices (upper case) and vectors (lower case)
$\{f_i\}$	A set of k frequencies ($k \leq n$), derived from a dataset $\{x_i\}$. If $\{x_i\}$ contains discrete values, some of which occur multiple times, then $\{f_i\}$ represents the number of occurrences or the count of each distinct value. $\{f_i\}$ may also represent the number of occurrences of values that lie in a range or set of ranges, $\{r_i\}$. If a dataset contains n values, then the sum $\sum f_i=n$. The set $\{f_i\}$ is often written as $f(x_i)$. If $\{f_i\}$ is regarded as a set of weights (for example attribute values) associated with the $\{x_i\}$, it may be written as the set $\{w_i\}$ or $w(x_i)$. If a set of frequencies, $\{f_i\}$, have been standardized by dividing each value f_i by their sum, $\sum f_i$ then $\{f_i\}$ may be regarded as a set of estimated probabilities and $\sum f_i=1$
$\sum$	Summation symbol, e.g. $x_1+x_2+x_3+\ldots+x_n$. If no limits are shown the sum is assumed to apply to all subsequent elements, otherwise upper and/or lower limits for summation are provided
$\cap$	Set intersection. The notation $P(A \cap B)$ is used to indicate the probability of A *and* B
$\cup$	Set union. The notation $P(A \cup B)$ is used to indicate the probability of A *or* B
Δ	Set symmetric difference. The set of objects in A that are not in B plus the set of objects in B that are not in A
$\int$	Integration symbol. If no limits are shown the sum is assumed to apply to all elements, otherwise upper and/or lower limits for integration are provided
$\prod$	Product symbol, e.g. $x_1 \cdot x_2 \cdot x_3 \cdot \ldots \cdot x_n$. If no limits are shown the product is assumed to apply to all subsequent elements, otherwise upper and/or lower limits for multiplication are provided
$\hat{}$	Hat or carat symbol: used in conjunction with Greek symbols (directly above) to indicate a value is an estimate of a parameter or the true population value
$\rightarrow$	Tends to, typically applied to indicate the limit as a variable tends to 0 or ∞

Item	Description
$\bar{}$	Solidus or overbar symbol: used directly above a variable to indicate a value is the mean of a set of sample values
~	Two meanings apply, depending on the context: (i) "is distributed as", for example y~N(0,1) means the variable y has a distribution that is Normal with a mean of 0 and standard deviation of 1; (ii) negation, as in ~A means NOT A, or sometimes referred to as the complement of A. Note that the R language uses this symbol when defining regression models
!	Factorial symbol. $z=n!$ means $z=n(n-1)(n-2)\ldots1$. $n>=0$. Note that 0! is defined as 1. Usually applied to integer values of n. May be defined for fractional values of n using the Gamma function. Note that for large n Stirling's approximation may be used. R: factorial(n) — computes $n!$; if a range is specified, for example 1:5 then all the factorials from 1 to 5 are computed
$\binom{n}{r}$	Binomial expansion coefficients, also written as ${}^{n}C_{r}$ or similar, and shorthand for $n!/[(n-r)!r!]$.
≡	'Equivalent to' symbol
≈	'Approximately equal to' symbol
∝	Proportional to
∈	'Belongs to' symbol, e.g. $x\in[0,2]$ means that x belongs to/is drawn from the set of all values in the closed interval [0,2]; $x\in\{0,1\}$ means that x can take the values 0 and 1
≤	Less than or equal to, represented in the text where necessary by <= (provided in this form to support display by some web browsers)
≥	Greater than or equal to, represented in the text where necessary by >= (provided in this form to support display by some web browsers)
$\lfloor x \rfloor$	Floor function. Interpreted as the largest integer value not greater than x. Sometimes, but not always, implemented in software as int(x), where int() is the integer part of a real valued variable
	Ceiling function. Interpreted as the smallest integer value not less than x. Sometimes, but not always, implemented in software as int(x+1), where int() is the integer part of a real valued variable
A|B	"given", as in P(A|B) is the probability of A given B or A *conditional upon* B

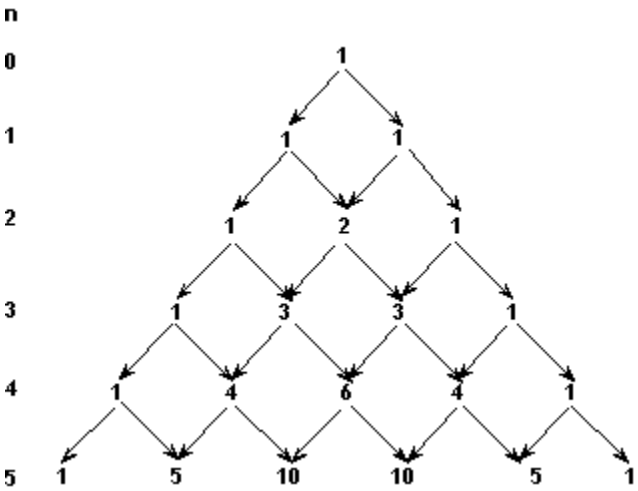
References

Wikipedia: Table of mathematical symbols: http://en.wikipedia.org/wiki/Table_of_mathematical_symbols

1.5 Historical context

Statistics is a relatively young discipline — for discussions on the history of statistics see Stigler (1986, [STI1]) and Newman (1960,[NEW1]). Much of the foundation work for the subject has been developed in the last 150 years, although its beginnings date back to the 13th century involving the expansion of the series $(p+q)^n$, for n=0,1,2.... The coefficients of this 'binomial' expansion were found to exhibit a well defined pattern (illustrated below) known as Pascal's triangle. Each coefficient can be obtained as the sum of the two immediately above in the diagram, as indicated.

Coefficients of the Binomial expansion



Pascal used this observation to produce a formula for the coefficients, which he noted was the same as the formula for the number of different combinations (or arrangements) of r events from a set of n (r=0,1,...n). , usually denoted:

$${}^{n}C_{r} \text{ or } \binom{n}{r}$$

This formula is typically expanded as:

$${}^{n}C_{r} = \frac{n!}{(n-r)!r!}$$

Hence with n=5, and noting that 0! is defined as 1, we have for r=[0,1,2,3,4,5] the values [1,5,10,10,5,1] as per Pascal's triangle, above. What this formula for the coefficients says, for example, is that are 5 different ways of arranging one p and four q's. These arrangements, or possible different combinations, are:

pqqqq, *qpqqq*, *qqpqq*, *qqqpq*, and *qqqqp*

and exactly the same is true if we took one *q* and four *p*'s. There is only one possible arrangement of all *p*'s or all *q*'s, but there are 10 possible combinations or sequences if there are 2 of one and 3 of the other. The possible different combinations are:

ppqqq, qppqq, qqppq, qqqpp, pqpqq, pqqpq, pqqqp, qpqpq, qpqqp, qqpqp

In these examples the order of arrangement is important, and we are interested in all possible *combinations*. If the order is not important the number of arrangements would be greater and the formula simplifies to counting the number of *permutations*:

$${}^{n}P_{r}=\frac{n!}{(n-r)!}$$

Assuming $(p+q)=1$ then clearly $(p+q)^n=1$. Jakob Bernoulli's theorem (published in 1713, after his death) states that if *p* is the probability of a single event occurring (e.g. a 2 being the result when a six-sided die is thrown), and *q* =1-*p* is the probability of it not occurring (e.g. the die showing any other value but 2) then the probability of the event occurring *at least m times* in *n* trials is the sum of all the terms of $(p+q)^n$ starting from the term with elements including p^r where $r \geq m$, i.e.

$$\sum_{r=m}^{n}\frac{n!}{r!(n-r)!}p^{r}q^{n-r}$$

So, if a die is thrown 5 times, the expected number of occasions a 2 will occur will be determined by the terms of the binomial expansion for which $p = 1/6$, and $q = 1-p = 5/6$):

$$p^0q^5, 5p^1q^4, 10p^2q^3, 10p^3q^2, 5p^4q^1, p^5q^0$$

which in this case give us the set of probabilities (to 3dp): 0.402,0.402,0.161,0.032,0.003,0.000. So the chance of throwing *at least one* "2" from 5 throws of an unbiased die is the sum of all the terms from $m=1$ to 5, i.e. roughly 60% (59.8%), and the chances of all 5 throws turning up as a 2 is almost zero. Notice that we could also have computed this result more directly as 1 minus the probability of no twos, which is $1-(1/6)^0(5/6)^5=1-0.402$, the same result as above.

This kind of computation, which is based on an *a priori* understanding of a problem in which the various outcomes are equally likely, works well in certain fields, such as games of chance — roulette, card games, dice games — but is not readily generalized to more complex and familiar problems. In most cases we do not know the exact chance of a particular event occurring, but we can obtain an estimate of this assuming we have a fairly large and *representative* sample of data. For example, if we collate data over a number of years on the age at which males and females die in a particular city, then one might use this information to provide an estimate of the probability that a woman of age 45 resident in that location will die within the next 12 months. This information, which is a form of *a posteriori* calculation of probability, is exactly the kind of approach that forms the basis for what are known as mortality tables, and these are used by the life insurance industry to guide the setting of insurance premiums. Statisticians involved in this particular field are called actuaries, and their principal task is to analyze collected data on all manner of events in order to produce probability estimates for a range of outcomes on which insurance premiums are then based. The collected data are typically called *statistics*, here being the plural form. The term *statistics* in the singular, refers to the science of how best to collect and analyze such data.

Returning to the games of chance examples above, we could approach the problem of determining the probability that at least one 2 is thrown from 5 separate throws of the die by conducting an experiment or *trial*. First, we could simply throw a die 5 times and count the number of times (if any) a 2 was the uppermost face. However, this would be a very small trial of just one set of throws. If we conducted many more trials, perhaps 1000 or more, we would get a better picture of the pattern of events. More specifically we could make a chart of the observed *frequency* of each type of event, where the possible events are: zero 2s, one 2, two 2s and so on up to five 2s. In practice, throwing a 6-sided die a very large number of times and counting the frequency with which each value appears is very time-consuming and difficult. Errors in the process will inevitably creep in: the physical die used is unlikely to be perfect, in the sense that differences in the shape of its corners and surfaces may lead some faces to be very slightly more likely to appear uppermost than others; as time goes on the die will wear, and this could affect the results; the process of throwing a die and the surface onto which the die is thrown may affect the results; over time we may make errors in the counting process, especially if the process continues for a very long time... in fact there are very many reasons for arguing that a physical approach is unlikely to work well.

As an alternative we can use a simple computer program with a random number generator, to simulate the throwing of a six-sided die. Although modern random number generators are extremely good, in that their randomness has been the subject of an enormous amount of testing and research, there will be a very slight bias using this approach, but it is safe to ignore this at present. In the table below we have run a simple simulation by generating a random integer number between the values of 1 and 6 a total of 100,000 times. Given that we expect each value to occur with a probability of 1/6, we would expect each value to appear approximately 16667 times. We can see that in this trial, the largest absolute difference between the simulated or observed frequency, f_o, and the *a priori* or expected frequency, f_e, is 203, which is around 1.2%.

Face	Frequency	|Observed-Expected|
1	16741	74
2	16870	203
3	16617	50
4	16635	32
5	16547	120
6	16589	78

This difference is either simply a matter of chance, or perhaps imperfections in the random number algorithm, or maybe in the simulation program. Some of this uncertainty can be removed by repeating the trial many times or using a larger number of tests in a single trial, and by checking the process using different software on different computers with different architectures. In our case we increased the trial run size to 1 million, and found that the largest percentage difference was 0.35%, suggesting that the random number generator and algorithm being used were indeed broadly unbiased, and also illustrating the so-called "Law of large numbers" or "Golden theorem", also due to Bernoulli. Essentially this law states that as the sample size is increased (towards infinity), the sample average tends to the true 'population' average. In the example of rolling a die, the possible values are 1,2,...6, the average of which is 3.5, so the long term average from a large number of trials should approach 3.5 arbitrarily closely. There are actually two variants of this law commonly recognized, the so-called Weak Law and the Strong Law, although the differences between these variants are quite subtle. Essentially the Weak Law allows for a

larger (possibly infinite) number of very small differences between the true average and the long term sampled average, whilst the Strong Law allows just for a finite number of such cases.

This example has not directly told us how likely we are to see one or more 2s when the die is thrown five times. In this case we have to simulate batches of 5 throws at a time, and count the proportion of these batches that have one or more 2s thrown. In this case we again compute 100,000 trials, each of which involves 5 throws (so 0.5 million iterations in total) and we find the following results from a sequence of such trials: 59753, 59767,59806,... each of which is very close to the expected value based on the percentage we derived earlier, more precisely 59812 (59.812%). In general it is unnecessary to manually or programmatically compute such probabilities for well-known distributions such as the Binomial, since almost all statistical software packages will perform the computation for you. For example, the Excel function BINOMDIST() could be used. Until relatively recently statistical tables, laboriously calculated by hand or with the aid of mechanical calculators, were the principal means of comparing observed results with standard distributions. Although this is no longer necessary the use of tables can be a quick and simple procedure, and we have therefore included a number of these in the Resources topic, Distribution tables section, of this Handbook.

A number of observations are worth making about the above example. First, although we are conducting a series of trials, and using the observed data to produce our probability estimates, the values we obtain vary. So there is a *distribution* of results, most of which are very close to our expected (true) value, but in a smaller number of cases the results we obtain might, by chance, be rather more divergent from the expected frequency. This pattern of divergence could be studied, and the proportion of trials that diverged from the expected value by more than 1%, 2% etc. could be plotted. We could then compare an observed result, say one that diverged by 7% from that expected, and ask "how likely is it that this difference is due to chance?". For example, if there was less than one chance in 20 (5%) of such a large divergence, we might decide the observed value was probably not a simple result of chance but more likely that some other factor was causing the observed variation. From the Law of Large Numbers we now know that the size of our sample or trial is important — smaller samples diverge more (in relative, not absolute, terms) than larger samples, so this kind of analysis must take into account sample size. Many real-world situations involve modest sized samples and trials, which may or may not be truly representative of the populations from which they are drawn. The subject of statistics provides specific techniques for addressing such questions, by drawing upon experiments and mathematical analyses that have examined a large range of commonly occurring questions and datasets.

A second observation about this example is that we have been able to compare our trials with a well-defined and known 'true value', which is not generally the situation encountered. In most cases we have to rely more heavily on the data and an understanding of similar experiments, in order to obtain some idea of the level of uncertainty or error associated with our findings.

A third, and less obvious observation, is that if our trial, experiments and/or computer simulations are in some way biased or incorrectly specified or incomplete, our results will also be of dubious value. In general it is quite difficult to be certain that such factors have not affected the observed results and therefore great care is needed when designing experiments or producing simulations.

Finally, it is important to recognize that a high proportion of datasets are not obtained from well-defined and controlled experiments, but are observations made and/or collections of data obtained, by third parties, often government agencies, with a whole host of known and unknown issues relating to their quality and how representative they are. Similarly, much data is collected on human populations and their behavior, whether this be medical research data, social surveys, analysis of purchasing behavior or voting intentions. Such datasets are,

almost by definition, simply observations on samples from a population taken at a particular point in time, in which the sampling units (individual people) are not fully understood or 'controlled' and can only loosely be regarded as members of a well-defined 'population'.

With the explosion in the availability of scientific data during the latter part of the 18th century and early 19th century, notably in the fields of navigation, geodesy and astronomy, efforts were made to identify associations and patterns that could be used to simplify the datasets. The aim was to minimize the error associated with large numbers of observations by examining the degree to which they fitted a simple model, such as a straight line or simple curve, and then to predict the behavior of the variables or system under examination based on this approximation. One of the first and perhaps most notable of these efforts was the discovery of the method of Least Squares, which Gauss reputedly devised at the age of 18. This method was independently discovered and developed by a number of other scientists, notably Legendre, and applied in a variety of different fields. In the case of statistical analysis, least squares is most commonly encountered in connection with linear and non-linear regression, but it was originally devised simply as the 'best' means of fitting an analytic curve (or straight line) to a set of data, in particular measurements of astronomical orbits.

During the course of the late 1900s and the first half of the 20th century major developments were made in many areas of statistics. A number of these are discussed in greater detail in the sections which follow, but of particular note is the work of a series of scientists and mathematicians working at University College London (UCL). This commenced in the 1860s with the research of the scientist Sir Francis Galton (a relation of Charles Darwin), who was investigating whether characteristics of the human population appeared to be acquired or inherited, and if inherited, whether humankind could be altered (improved) by selective breeding (a highly controversial scientific discipline, known as Eugenics). The complexity of this task led Galton to develop the concepts of correlation and regression, which were subsequently developed by Karl Pearson and refined by his student, G Udny Yule, who delivered an influential series of annual lectures on statistics at UCL which became the foundation of his famous book, An Introduction to the Theory of Statistics [YUL1], first published in 1911. Another student of Pearson at UCL was a young chemist, William Gosset, who worked for the brewing business, Guinness. He is best known for his work on testing data that have been obtained from relatively small samples. Owing to restrictions imposed by his employers on publishing his work under his own name, he used the pseudonym "Student", from which the well-known "Students t-test" and the t-distribution arise. Also joining UCL for 10 years as Professor of Eugenics, was R A Fisher, perhaps the most important and influential statistician of the 20th century. Fisher's contributions were many, but he is perhaps most famous for his work on the Design of Experiments [FIS1], a field which is central to the conduct of controlled experiments such as agricultural and medical trials. Also at UCL, but working in a different field, psychology, Charles Spearman was responsible for the introduction of a number of statistical techniques including Rank Correlation and Factor Analysis. And lastly, but not least, two eminent statisticians: Austin Bradford Hill, whose work we discuss in the section on statistics in medical research, attended Pearson's lectures at UCL and drew on many of the ideas presented in developing his formative work on the application of statistics to medical research; and George Box, developer of much of the subject we now refer to as industrial statistics. Aspects of his work are included in our discussion of the Design of Experiments, especially factorial designs.

Substantial changes to the conduct of statistical analysis have come with the rise of computers, automated monitoring and tracking technologies (e.g. GPS, smartcard systems etc.) and the Internet. The computer has removed the need for statistical tables and, to a large extent, the need to be able to recall and compute many of the complex expressions used in statistical analysis. They have also enabled very large volumes of data to be stored and analyzed, which itself presents a whole new set of challenges and opportunities. To meet some of

these, scientists such as John Tukey and others developed the concept of Exploratory Data Analysis, or "EDA", which can be described as a set of visualization tools and exploratory methods designed to help researchers understand large and complex datasets, picking out significant features and feature combinations for further study. This field has become one of the most active areas of research and development in recent years, spreading well beyond the confines of the statistical fraternity, with new techniques such as Data Mining, 3D visualizations, Exploratory Spatio-Temporal Data Analysis (ESTDA) and a whole host of other procedures becoming widely used. A further, equally important impact of computational power, we have already glimpsed in our discussion on games of chance — it is possible to use computers to undertake large-scale simulations for a range of purposes, amongst the most important of which is the generation of pseudo-probability distributions for problems for which closed mathematical solutions are not possible or where the complexity of the constraints or environmental factors make simulation and/or randomization approaches the only viable option.

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1.6 An applications-led discipline

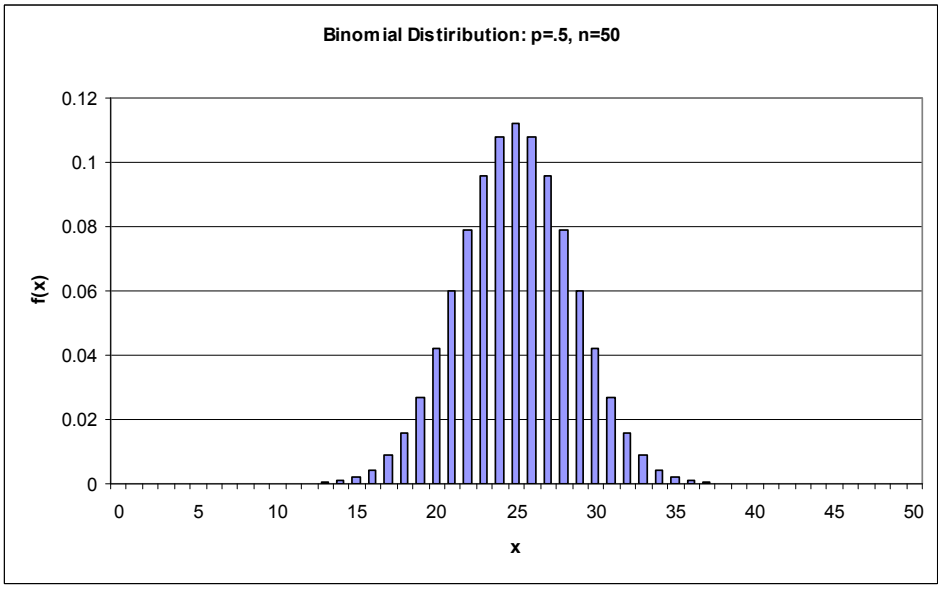
As mentioned in the previous section, the discipline that we now know as Statistics, developed from early work in a number of applied fields. It was, and is, very much an applied science. Gambling was undoubtedly one of the most important early drivers of research into probability and statistical methods and Abraham De Moivre's book, published in 1718, "The Doctrine of Chance: A method of calculating the probabilities of events in play" [DEM1] was essential reading for any serious gambler at the time. The book contained an explanation of the basic ideas of probability, including permutations and combinations, together with detailed analysis of a variety of games of chance, including card games with delightful names such as Basette and Pharaon (Faro), games of dice, roulette, lotteries etc. A typical entry in De Moivre's book is as follows:

"Suppose there is a heap of 13 cards of one color [suit], and another heap of 13 cards of another color; what is the Probability, that taking one Card at a venture [random] out of each heap, I shall take out the two Aces?" He then goes on to explain that since there is only one Ace in each heap, the separate probabilities are 1/13 and 1/13, so the combined probability (since the cards are independently drawn) is simply:

$$\frac{1}{13} \times \frac{1}{13} = \frac{1}{169}$$

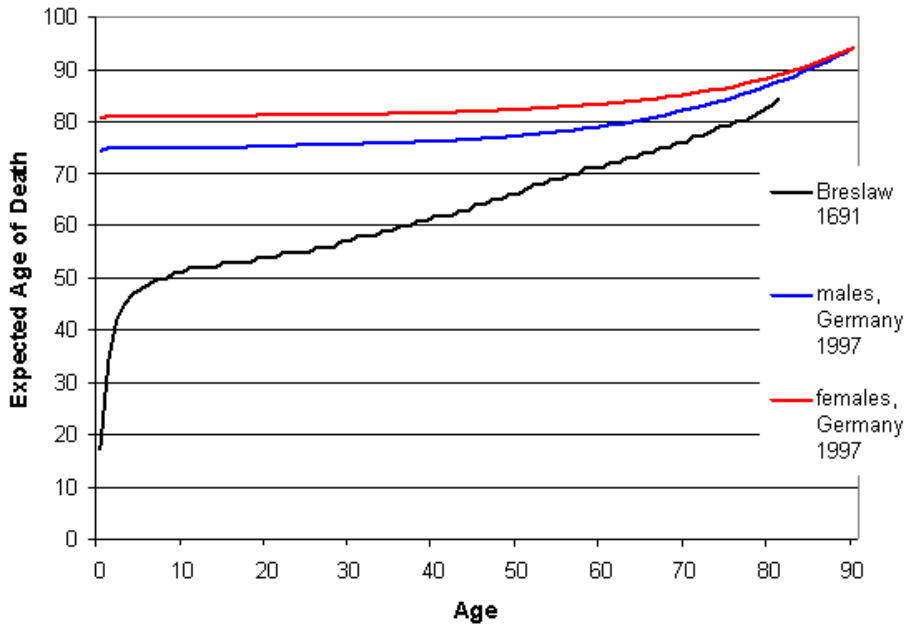
hence the chance of not drawing two Aces is 168/169, or put another way, the *odds* against drawing two Aces are 168:1 — for gambling, whether the gambler or the gambling house, setting and estimating such odds is vitally important! De Moivre's book ran into many editions, and it was in the revised 1738 and 1756 editions that De Moivre introduced a series approximation to the Binomial for large n with p and q not small (e.g. not less than 0.3). These conditions lead to an approximation that is generally known as the Normal distribution. His motivation for so developing this approximation was that computation of the terms of the Binomial for large values of n (e.g. 50+, as illustrated below) was extremely tedious and unrealistic to contemplate at that time.

Binomial distribution, mean = 25



Furthermore, as *n* increases the individual events have very small probabilities (with *n*=500 the maximum probability for an individual event with *p*=0.5 is 0.036 — i.e. there is just under 4% chance of seeing exactly 250 heads, say, when 500 tosses of an unbiased coin are made). For this reason one tends to be interested in the probability of seeing a group or range of values (e.g. 400 or more heads from 500 tosses), rather than any specific value. Looking at the chart the vertical bars should really be just vertical lines, and as the number of such lines becomes very large and the interval between events becomes relatively smaller, a continuous smooth bell-like curve approximation (which is what the Normal distribution provides) starts to make sense (see further, the Normal distribution).

De Moivre also worked extensively on another topic, mentioned in the previous section, mortality tables. This work developed following the publication by John Graunt in 1662 of figures on births and deaths in London, and similar research by Edmund Halley (the astronomer) of birth and deaths data for the City of Breslau (modern day Wrocław in Poland) between 1687 and 1691 [HAL1]. Halley was interested in using this data in order to "ascertain the price of annuities upon lives", i.e. to determine the level at which life insurance premiums (or *annuities*) might be set. As an illustration, Halley observed that (based on his data) there was only 100:1 chance that a man in Breslau aged 20 would die in the following 12 months (i.e. before reaching 21), but 38:1 if the man was 50 years old. A diagram derived from the data in Halley's publication of 1693 is shown below. De Moivre included Halley's data and sample annuity problems and solutions in the 1756 edition of his "Doctrine of Chance" book, cited above.



A very different application of statistics arose during the 19th century with the development of new forms of communication, especially the development of telephony and the introduction of manual and then mechanical exchange equipment. A Danish mathematician, Agner Erlang, working for the Copenhagen Telephone Authority (KTAS), addressed the important questions of queuing and congestion. Answers were needed to questions such as "how many operators are needed to service telephone calls for 1000 customers?" and "how many lines are required to ensure that 95% of our customers can call other major towns in the country without finding that the line is busy". Questions such as these are closely related to problems of queuing and queue management, such as "how many checkouts do I need in a supermarket to ensure customers on a busy Saturday do not have to wait in line more than a certain amount of time?", or "how long should we have a stop sign on red before we allow the traffic to cross an intersection?". Erlang investigated these questions by assuming that there are a large number of customers but only a small chance that any particular customer would be trying to make a call at any one time. This is rather like the Binomial with n large and p very small, which had been shown by the French mathematician, Siméon Poisson (in a work of 1837) to have a simple approximation, and is now given the name Poisson Distribution. Erlang also assumed that when a call was made, the call lengths followed an Exponential Distribution, so short calls were much more common than very long calls. In fact, this assumption is unnecessary – all that really matters is that the calls are made independently and have a known average duration over an interval of time, e.g. during the peak hour in the morning. The number of calls per hour made to the system times their average length gives the total *traffic*, in dimensionless units that are now called Erlangs and usually denoted by the letter A or E. Erlang derived a variety of statistical measures based on these assumptions, one of the most important being the so-called Grade of Service (GoS). This states the probability that a call will be rejected because the service is busy, where the traffic offered is E and the number of lines or operators etc available is m. The formula he derived, generally known as the Erlang B formula, is:

$$GoS = \frac{E^m / m!}{\sum_{k=0}^{m} E^k / k!}$$

Hence, if we have 2 units of traffic per hour (E=2) and m=5 channels to serve the traffic, the probability of congestion is expected to be just under 4%. Put another way, if you are designing facilities to serve a known peak traffic E and a target GoS of 5%, you can apply the formula incrementally (increasing m by 1 progressively) until you reach your target. Note that this very simple example assumes that there is no facility for putting calls into a queuing system, or re-routing them elsewhere, and critically assumes that calls arrive independently. In practice these assumptions worked very well for many years while telephone call traffic levels were quite low and stable over periods of 0.5-1.0 hours. However, with sudden increases in call rates people started to find lines busy and then called back immediately, with the result that call arrival rates were no longer random and independent (Poisson-like). This leads to a very rapidly degrading service levels and/or growing queuing patterns (familiar problems in physical examples such as supermarket checkouts and busy motorways, but also applicable to telephone and data communications networks). Erlang, and subsequently others, developed statistical formulas for addressing many questions of this type that are still used today. However, as with some other areas of statistical methods previously described, the rise of computational power has enabled entire systems to be simulated, allowing a range of complex conditions to be modeled and stress-tested, such as varying call arrival rates, allowing buffering (limited or unlimited), handling device failure and similar factors, introducing dynamic solutions based on responsive technology that would have been previously impossible to model analytically.

The final area of application we shall discuss is that of experimental design. Research into the best way to examine the effectiveness of different treatments applied to crops led R A Fisher to devise a whole family of scientific methods for addressing such problems. In 1919 Fisher joined the Rothamsted Agricultural Experiment Station and commenced work on the formal methods of randomization and the analysis of variance, which now form the basis for the design of 'controlled' experiments throughout the world. Examples of the kind of problem his procedures address are: "does a new fertilizer treatment X, under a range of different conditions/soils etc, improve the yield of crop Y?" or "a sample of women aged 50-60 are prescribed one of three treatments: hormone replacement therapy (HRT); or a placebo; or no HRT for x years — does the use of HRT significantly increase the risk of breast cancer?".

As can be seen from these varied example, statistics is a science that has developed from the need to address very specific and practical problems. The methods and measures developed over the last 150-200 years form the basis for the many of the standard procedures applied today, and are implemented in the numerous software packages and libraries utilized by researchers on a daily basis. What has perhaps changed in recent years is the growing use of computational methods to enable a broader range of problems, with more variables and much larger datasets to be analyzed. The range of applications now embraced by statistics is immense. As an indication of this spread, the following is a list of areas of specialism for consultants, as listed by the websites of the UK Royal Statistical Society (RSS): and the US American Statistical Association (ASA):

Statistical Consultancy — Areas of specialism — RSS

Applied operational research	Epidemiology	Neural networks and genetic algorithms	Sampling
Bayesian methods	Expert systems	Non-parametric statistics	Simulation
Bioassay	Exploratory data analysis	Numerical analysis and optimization	Spatial statistics
Calibration	Forecasting	Pattern recognition and image analysis	Statistical computing
Censuses and surveys	GLMs and other non-linear models	Quality methodology	Statistical inference
Clinical trials	Graphics	Probability	Survival analysis
Design & analysis of experiments	Multivariate analysis	Reliability	Time Series

Statistical Consultancy — Areas of specialism — ASA

Bayesian Methods	General Advanced Methodological Techniques	Quality Management, 6-Sigma	Statistical Software — SAS
Biometrics & Biostatistics	Graphics	Risk Assessment & Analysis	Statistical Software — SPSS
Construction of Tests & Measurements	Market Research	Sampling & Sample Design	Statistical Training
Data Collection Procedures	Modeling & Forecasting	Segmentation	Survey Design & Analysis
Decision Theory	Non Parametric Statistics	Statistical Organization & Administration	Systems Analysis & Programming
Experimental Design	Operations research	Statistical Process Control	Technical Writing & Editing
Expert Witness	Probability	Statistical Software — other	Temporal & Spatial Statistics

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Chapter 2

2 Statistical data

Statistics (plural) is the field of science that involves the collection, analysis and reporting of information that has been sampled from the world around us. The term *sampled* is important here. In most instances the data we analyze is a sample (a carefully selected representative subset) from a much larger *population*. In a production process, for example, the population might be the set of integrated circuit devices produced by a specific production line on a given day (perhaps 10,000 devices) and a sample would be a selection of a much smaller number of devices from this population (e.g. a sample of 100, to be tested for reliability). In general this sample should be arranged in such a way as to ensure that every chip from the population has an equal chance of being selected. Typically this is achieved by deciding on the number of items to sample, and then using equi-probable random numbers to choose the particular devices to be tested from the labeled population members. The details of this sampling process, and the sample size required, is discussed in the section Sampling and sample size.

The term *statistic* (singular) refers to a value or quantity, such as the mean value, maximum or total, calculated from a sample. Such values may be used to estimate the (presumed) *population* value of that statistic. Such population values, particular key values such as the mean and variance, are known as *parameters* of the pattern or *distribution* of population values.

In many instances the question of what constitutes the population is not as clear as suggested above. When undertaking surveys of householders, the total population is rarely known, although an estimate of the population size may be available. Likewise, when undertaking field research, taking measurements of soil contaminants, or air pollutants or using remote sensing data, the population being investigated is often not so well-defined and may be infinite. When examining a particular natural or man made *process*, the set of outcomes of the process may be considered as the population, so the process outcomes are effectively the population.

Since statistics involves the analysis of data, and the process of obtaining data involves some kind of measurement process, a good understanding of measurement is important. In the subsections that follow, we discuss the question of measurement and measurement scales, and how measured data can be grouped into simple classes to be produce data distributions. Finally we introduce two issues that serve to disguise or alter the results of measurement in somewhat unexpected ways. The first of these is the so-called statistical grouping affect, whereby grouped data produce results that differ from ungrouped data in a non-obvious manner. The second of these is a spatial effect, whereby selection of particular arrangement of spatial groupings (such as census districts) can radically alter the results one obtains.

Perhaps one of the mostly hotly debated topics in recent years has been the rise of so-called "Big Data". In an article "Big Data: Are we making a big mistake?" in the Financial Times, March 2014, Tim Harford addresses these issues and more, highlighting some of the less obvious issues posed by Big Data. Perhaps primary amongst these is the bias that is found in many such datasets. Such biases may be subtle and difficult to identify and impossible to manage. For example, almost all Internet-related Big Data is intrinsically biased in favor of those who have access to and utilize the Internet most, with demographic and geographic bias built-in. The same applies for specific services, such as Google, Twitter, Facebook, mobile phone networks, opt-in online surveys, opt-in emails — the examples are many and varied, but the problems are much the same as those familiar to statisticians for over a century. Big Data does not imply good data or unbiased data, and Big Data presents other problems — it is all to easy to focus on the data exploration and pattern discovery, identifying correlations that may well be spurious — a result of the sheer volume of data and the number of events and variables measured. With enough data and

enough comparisons, statistically significant findings are inevitable, but that does not necessarily provide real insights, understanding, or identification of causal relationships. Of course there are many important and interesting datasets where the collection and storage is far more systematic, less subject to bias, recording variables in a direct manner, with 'complete' and 'clean' records. Such data are stored and managed well and tend to be those collected by agencies who supplement the data with metadata (data about data) and quality assurance information.

Measurement

In principle the process of measurement should seek to ensure that results obtained are consistent, accurate (a term that requires separate discussion), representative, and if necessary independently reproducible. Some factors of particular importance include:

- **framework** — the process of producing measurements is both a technical and, to an extent, philosophical exercise. The technical framework involves the set of tools and procedures used to obtain and store numerical data regarding the entities being measured. Different technical frameworks may produce different data of varying quality from the same set of entities. In many instances measurement is made relative to some internationally agreed standard, such as the meter (for length) or the kilogram (for mass). The philosophical framework involves the notion that a meaningful numerical value or set of values can be assigned (using some technical framework) to attributes of the entities. This is a model or representation of these entity attributes in the form of numerical data — a person's height is an attribute that we can observe visually, describe in words, or assign a number to based on an agreed procedure relative to a standard (in meters, which in turn is based on the agreed measurement of the speed of light in a vacuum)
- **observer effects** — in both social and pure science research, observer effects can be significant. As a simple example, if we are interested in measuring the temperature and air quality in a process clean room, the presence of a person taking such measurements would inevitably have some affect on the readings. Similarly, in social research many programmes can display the so-called Hawthorne Effect in which changes (often improvements) in performance are partially or wholly the result of behavioral changes in the presence of the observer (reflecting greater interest in the individuals being observed)
- **metrics** — when measuring distance in the plane using Euclidean measure the results are invariant under translation, reflection and rotation. So if we use Euclidean measure we can safely make measurements of distances over relatively small areas and not worry about the location or orientation at which we took the measurements and made the calculation. However, over larger areas and/or using a different metric, measurements may fail the invariance test. In the case of measurements that seek to compute distances, measurements made using the so-called City block or Manhattan distance are not invariant under rotation. Likewise, Euclidean distance measurements give incorrect results over larger distances on the Earth's surface (e.g. >20 kilometers). When making other forms of measurement similar issues apply (e.g. the effect of the local gravitational field on weight, the local magnetic field on magnetic flux, etc.)
- **temporal effects** — measurement made at different times of the day, days of the year and in different years will inevitably differ. If the differences are simply random fluctuations in a broadly constant process (results are unaffected by temporal translation of the data) the process is described as being *stationary*. If a trend exists (which could be linear, cyclical or some other pattern) the process is said to be *non-stationary*. All too often consideration of the temporal aspect of measurement is omitted, e.g. a person's height will be measured as shorter in the evening as compared with the morning, a persons academic or sporting achievement can be significantly affected by when they were born (see Gladwell, 2008, for an extensive discussion of this issue,

[GLA1]) — the issue is always present even if it is not of direct concern. Frequently the sequence of event measurement is important, especially where humans are doing the measurements or recordings, since issues such as concentration become important over time; event sequences may also be explicitly monitored, as in control charts, time series analysis and neural network learning

- **spatial effects** — measurements made at different locations will typically exhibit spatial variation. If all locations provided identical data the results would be a spatially uniform distribution. If the results are similar in all directions at all locations, then the process is described as *isotropic* (i.e. results are rotationally invariant). If the results are similar at all locations (i.e. the results are translationally invariant) then the process can be described as stationary. In practice most spatial datasets are non-stationary

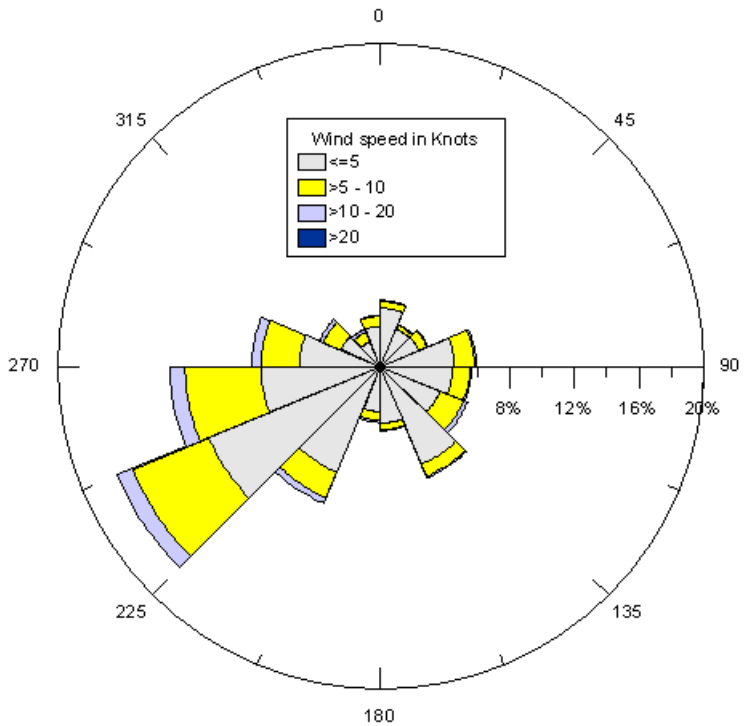
Measurement scales

Measurement gives rise to values, such as counts, sets of decimal values, binary responses (yes/no, presence/absence) etc., which may be of different types (scales). The principal scales encountered are:

- **Nominal** (or Categorical): data is really just assignment to named classes, such as Red, Blue, Green — or Utah, Nevada, New York. An attribute is nominal if it successfully distinguishes between groups, but without any implied ranking or potential for arithmetic. For example, a telephone number can be a useful attribute of a place, but the number itself generally has no numeric meaning. It would make no sense to add or divide telephone numbers, and there is no sense in which the number 9680244 is more or better than the number 8938049. Likewise, assigning arbitrary numerical values to classes of land type, e.g. 1=arable, 2=woodland, 3=marsh, 4=other is simply a convenient form of naming (the values are still nominal)
- **Ordinal**: this term refers to data values that involves a concept of order, from least to greatest and may include negative numbers and 0. A set of apparently ordered categories such as: 1=low, 2=medium, 3=high, 4="don't know" does not form an ordinal scale. An attribute is ordinal if it implies a ranking, in the sense that Class 1 may be better than Class 2, but as with nominal attributes arithmetic operations do not make sense, and there is no implication that Class 3 is worse than Class 2 by the precise amount by which Class 2 is worse than Class 1. An example of an ordinal scale might be preferred locations for residences — an individual may prefer some areas of a city to others, but such differences between areas may be barely noticeable or quite profound. Analysis of nominal and ordinal data is often qualitative, or uses visualization techniques to highlight interesting patterns, and may use non-parametric statistical methods especially when count data are available
- **Interval**: numeric data that exhibits order, plus the ability to measure the interval (distance) between any pair of objects on the scale (e.g. $2x\text{-}x \equiv 3x\text{-}2x$). Data are of interval type if differences make sense, as they do for example with measurements of temperature on the Celsius or Fahrenheit scales
- **Ratio**: interval plus a natural origin, e.g. temperature in degrees Kelvin, weights of people (i.e. so $x=2y$ is meaningful); Interval or ratio scales are required for most forms of (parametric) statistical analysis. Data are ratio scaled if it makes sense to divide one measurement by another. For example, it makes sense to say that one person weighs twice as much as another person, but it makes no sense to say that a temperature of 20 Celsius is twice as warm as a temperature of 10 Celsius, because while weight has a meaningful absolute zero Celsius temperature does not (but on an absolute scale of temperature, such as the Kelvin scale, 200 degrees can indeed be said to be twice as warm as 100 degrees). It follows that negative values cannot exist on a ratio scale.
- **Cyclic**: modulo data — like angles and clock time. Measurements of attributes that represent directions or cyclic phenomena have the awkward property that two distinct points on the scale can be equal — for example, 0 and

360 degrees. Directional data are cyclic (see the sample *wind rose* diagram below) as are calendar dates. Arithmetic operations are problematic with cyclic data, and special techniques are needed to handle them. For example, it makes no sense to average 1° and 359° to get 180°, since the average of two directions close to north clearly is not south. Mardia and Jupp (1999, [MAR1]) provide a comprehensive review of the analysis of directional or cyclic data

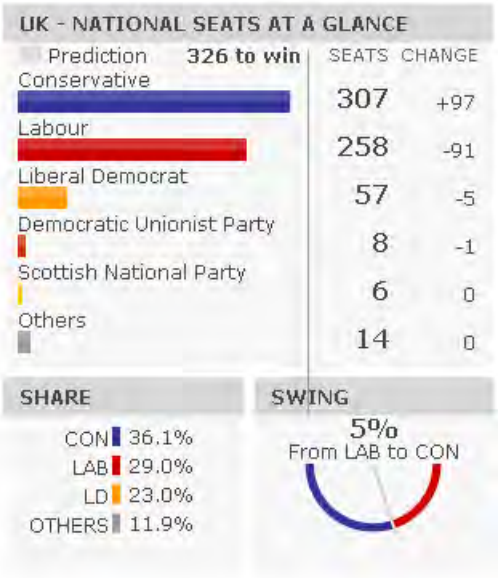
Cyclic data — Wind direction and speed, single location

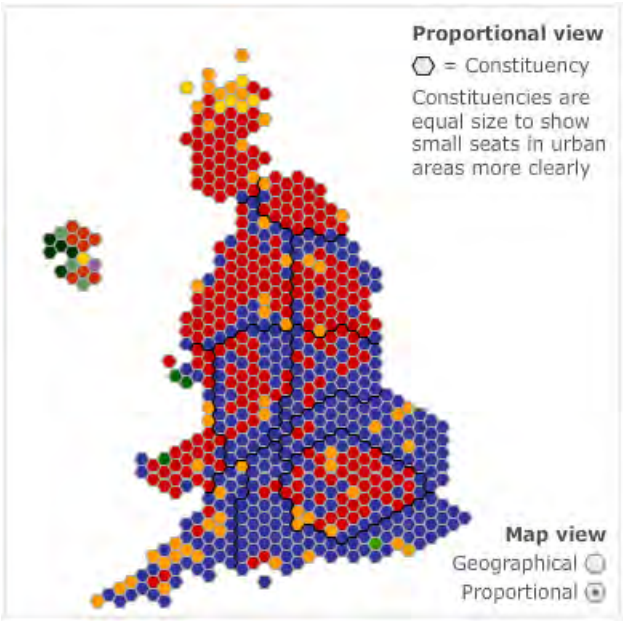


Bar charts, Histograms and Frequency distributions

- **Bar chart**: The process of measurement may produce data that are recorded as counts and assigned to purely nominal classes, for example counts of different bird species in a woodland. In this instance a simple bar chart may be produced to illustrate the different relative frequencies of each species. Each class is assigned an individual vertical or horizontal bar and typically each bar being the same width (so height indicates relative frequency). Bars are separated by distinct gaps and the order in which the bars are placed on the horizontal or vertical axis is of no importance. The example below (upper diagram) shows the results of the UK parliamentary election in May 2010. The bar chart indicates the seats one in the "first past the post" system used currently in the UK, with a geographic map of the spread of these results. The lower diagram shows the same data but with the geography amended to minimize the visual distortion caused by constituencies having very different areas. For color versions of these charts see the web or PDF editions of this Handbook.

BBC UK Election 2010 results





source: http://news.bbc.co.uk/1/shared/election2010/results/. Note that the first diagram is familiar but misleading as it does not reflect the density of voters, suggesting the seats obtained by parties in large rural areas are somehow more significant than densely populated urban areas. This view can be corrected in various ways, most simply by adjusting the areas to reflect the populations in each. The result is a proportional map, with areas distorted but still recognizable, as illustrated in the second diagram.

- **Histogram**: If measurements yield numerical values on an interval or ratio scale, these can be grouped into classes and the counts (or frequencies) in each class plotted as a bar chart in which the order on the horizontal axis (or *x*-axis) is important. A bar chart of this type is called a *histogram* and should be plotted without spaces between the vertical bars reflecting the continuous nature of the scale (see example of light bulb life data, below). The term histogram was introduced by Karl Pearson in the late 19th century to describe any chart of

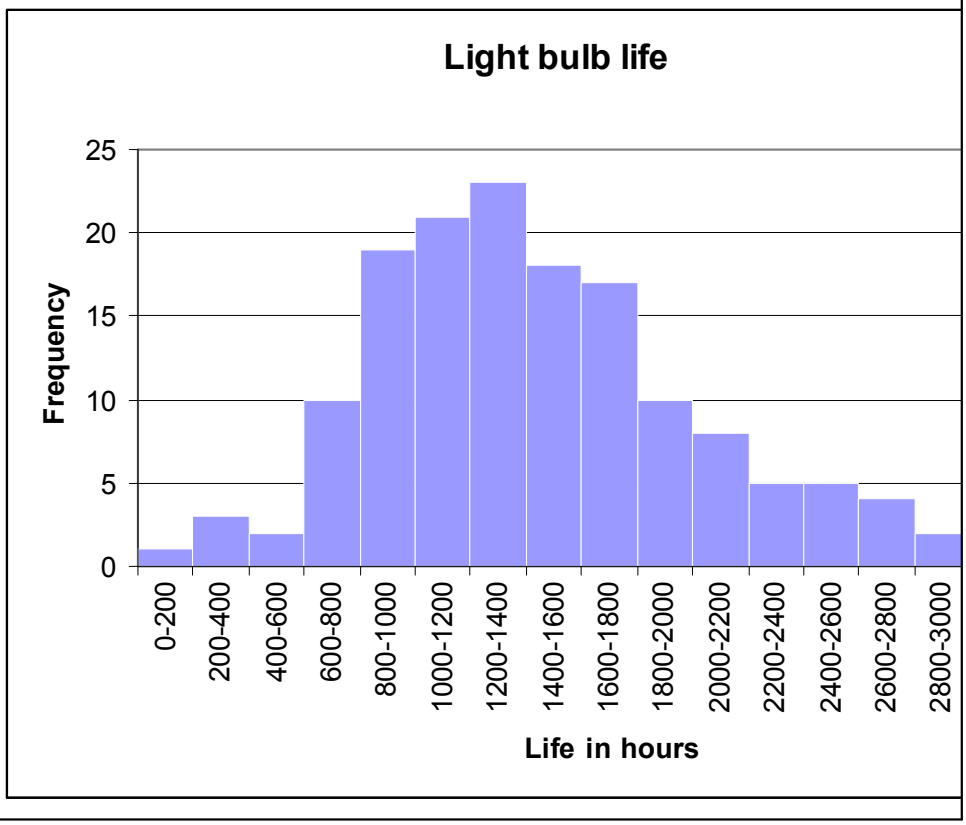
this type, especially charts in which the horizontal axis represented time. He liked the idea that the Greek word *histos*, which means anything placed vertically, like a ship's mast, is similar to the word *historical*, giving the idea of a frequency chart with a time-based *x*-axis..

- **Frequency distribution**: A frequency distribution is a tabulated set of sample data, showing the number of occurrences of events or observations that fall into distinct classes or that have particular values. As such, it can be seen as a convenient way of avoiding the need to list every data item observed separately. However, frequency distributions can often provide greater insight into the pattern of sample values, and enables these patterns to be compared with well-understood standard distributions, such as the Binomial (discrete) and Normal (continuous) distribution. A simple example is shown in the table below together with the chart (or histogram) of the data. In this table there are 17 equal interval classes, for each of which the number of light bulbs in a sample of *N*=150 that fail after a certain time are listed.

Length of life of electric light bulbs — tabulated and histogram

Life (hours)	Frequency
0-200	1
200-400	3
400-600	2
600-800	10
800-1000	19
1000-1200	21
1200-1400	23
1400-1600	18
1600-1800	17
1800-2000	10
2000-2200	8
2200-2400	5
2400-2600	5
2600-2800	4
2800-3000	2
3000-3200	1
3200-3400	1
Total	150

Histogram of frequencies



after Pearson E S (1933, [PEA1])

Several observations should be made about this particular frequency distribution:

(i) it has a single category or *class* containing the most frequent bulb life (1200-1400hrs) — this category is called the mode, and because there is a single mode, the distribution is said to be *unimodal*

(ii) the set of classes in the tabulated list are not really correctly defined — the boundaries are indeterminate, and should be specified as [0,199.9],[200-399.9], etc (or similar) or better still [0,<200], [200,<400] etc (in Pearson's paper, which was primarily concerned with production control and sampling, he actually only supplied the frequency diagram, not the tabulated data) — the precise definition of the boundaries of classes avoids the problem of deciding how to assign values that lie on the boundary (e.g. a bulb with measured lifespan of exactly 200 hours)

(iii) each class is the same width (duration) and every data value is allocated to a unique class; however, when performing certain calculations, such as computing the mean value, a decision has to be made as to whether to use the recorded frequencies in the various classes or *bins*, or the source data (if available). If the frequencies have to be used, it is necessary to define a representative value for each interval, which is usually taken to be the mid-interval value. Note that this assumption hides the within-class variation in values which may create some errors in computations, especially if the class widths are large. The question of bin selection is discussed later in this section

(iv) the width (duration) of each class is somewhat arbitrary and this choice significantly affects the form of the frequency distribution. If the class width was very small (1 hour say) most classes would contain the frequency 0, and a few would contain just 1 failure. At the opposite extreme, if the class width was 3400 hours all the results would be in just the one class. In both these examples very little information would be gained from inspecting the pattern of frequencies. Selecting the class boundaries and number of classes is an important operation — it should ensure that the minimum of information is lost, whilst also ensuring that the distribution communicates useful and relevant information. Many authors recommend the use of an odd number of classes, and there are a myriad of rules-of-thumb for choosing the number of classes and class boundaries (see Class Intervals, below)

(v) all the data fits into the classes (in this example). This is often not possible to achieve with equal interval classes, especially at the upper and lower ends of the distribution. Indeed, frequency distributions with very long tails are common, and often the final category is taken as 3000+ for example

(vi) the data being analyzed in this example can be regarded as a continuous variable (lifespan of the bulb) and is a single variable (i.e. univariate data)

There are several extensions and variations that can be applied to the above model. The first is to rescale the vertical axis by dividing each class value by the total sample size (N=150), in which case the data are described as *relative frequencies*, and in examples such as this, the values can be considered as *estimated probabilities*.

A second important variant is the extension of the frequency table and chart to multivariate and multi-dimensional cases. In the bivariate case the data may simply be separate measures applied to the same classes, or they may be joint measures. For example, suppose that our classes show the heights of individuals in a large representative sample. The first column of a bivariate frequency tabulation might show the frequency distribution for men over 18 years, whilst the second column shows the same data but for women. However, if the mix of those sampled included fathers and sons, one could construct a two-way or *joint* frequency distribution (or *cross-tabulation*) of the men with classes "Tall" and "Short", where Tall is taken as over some agreed height. The table below illustrates such a cross-tabulation, based on a study of families carried out by Karl Pearson and Dr Alice Lee from 1893 onwards:

Cross-tabulation of father-son height data

	Father short	Father tall	Total fathers
Son short	250	89	339
Son tall	215	446	661
Total sons	465	535	1000

simplified, after K Pearson and A Lee (1903, Table XXII [PEA2]; the overall sample size of 1000 families and the cell entries are simply a proportional reduction from the 1078 cases in the original data).

In this example each part of the frequency distribution is divided into just 2 classes, but each could readily have been separated into 3 or more height bands. Indeed, the original table is divided into 20 rows and 17 columns (illustrated in full in the Probability section of this Handbook), but inevitably many of the table entries are blank. Row and column totals have been provided, and these are sometimes referred to as *marginal frequencies* or *marginal distributions*. They are essentially the univariate frequency distributions for the rows and columns taken separately.

As with the univariate frequency data, this table could be converted to relative frequencies by dividing through by 1000, but it also affords another perspective on the data; we can consider questions such as: "what is the probability that a tall son has a tall father?" If the data are truly representative of the population of fathers and sons, then the estimated probability is 446/1000 or 44.6%. But when we examine the table, we find that there are far more tall fathers and tall sons than short fathers and short sons. We could then ask "does this estimate of probability suggest that tall fathers have tall sons, i.e. some genetic or other relationship factor?". Overall we can see from the *totals* entries that 53.5% of our sample fathers are tall and 66.1% of the sons are tall, and if these two groups were completely independent we might reasonably expect 53.5% x 66.1% of the father-son combinations to be tall (applying the rule of multiplication for independent probabilities). But this combination is actually only 35.4%, so the 44.6% finding does suggest a relationship, but whether it is significant (i.e. highly unlikely to be a chance result) requires more careful analysis using a particular statistical technique, contingency table analysis. Cross-classifications of this kind do not require numeric classes or classes derived from numeric values as in this example — in many instances the rows contain classes such as "Success, Failure" or "Survived, Died" and the columns might contain "Treatment A, Treatment B, Placebo, No treatment", with the table entries providing a count of the number of plants, patients etc. recorded in that combination of classes. In general such multivariate classification tables are restricted to 2-way, and occasionally 3-way analysis, and rarely are the number of classes in each dimension of the classification large if analyzed in this manner — often they are 5 or less.

Frequency distributions can also by multi-dimensional. For example, the distribution of cases of a particular disease around a point source of contamination might be measured in distance bands and radial sectors around this location. This pattern might then be compared with a known bivariate frequency distribution, such as the bivariate Normal distribution. In three dimensions one could be looking at the distribution of bacteria in cheese, or the distribution of stars in a region of space.

Class intervals, bins and univariate classification

If sampled data are measurements of a continuous variable, *x*, such as the light bulb lifespans described above, then the standard procedure in frequency chart (or histogram) production is to create a set of equal width class

intervals (or *bins*) and count the frequencies occurring in each interval. The values at which the bins are separated are often referred to as *cut-points*. The number of intervals to be used is a matter for the researcher to determine, depending on the problem requirements. It is often helped, in interactive software packages, by viewing a display of the resulting histogram as different options are selected. For visualization purposes it is desirable to limit the number of classes to between 5 or 9, as using large numbers of classes (20+) can be difficult to display and interpret with clarity, and an odd number of intervals will ensure there is a central class. On the other hand, with a large set of observations that exhibit considerable spread across the range, a larger number of classes may be more helpful and will avoid the problem of having much of the real variation hidden by large class intervals.

There are several rules of thumb for determining the ideal number of bins and/or the width for fixed-width bins for real-valued continuous data. These include the following (*n* is the number of observations or data items to be grouped, *k* is the number of classes, *h* is the bin width, *s* is the standardized average spread or standard deviation of the sample data):

$$k = \left\lceil \frac{\max - \min}{h} \right\rceil, \text{ or } h = \left\lceil \frac{\max - \min}{k} \right\rceil$$

These options use the range and a pre-selected bin width to define the number of bins, *k*, or alternatively the number of bins is specified and the range used to determine the bin width, *h*. Note that if the distribution has a very long tail, e.g. a few data items that are very much larger or smaller than all the others, these formulas will produce excessively wide bins.

The next formula is due to Scott (1979, [SCO1]) and uses the standard deviation of the dataset, *s*, rather than the range to determine bin width:

$$h = \left\lceil 3.5s / n^{1/3} \right\rceil$$

Thus for 1000 data items with a standard deviation of 25, *h*=9. The number of bins still remains to be chosen, and this will be a matter of choice again, but could safely use the range calculation for *k*, above, in most cases. Scott's model is built on an analysis of the optimal properties of a binning arrangement with constant bin widths and an examination of the ideas of so-called kernel density estimation (KDE) techniques. The latter use all the data points to create a smooth estimated probability distribution (or probability density function), which has been shown to produce excellent results but may require a considerable amount of data processing.

As mentioned earlier, if the frequencies are to be used in computations it is necessary to define a representative value for each interval, which is usually taken to be the mid-interval value. Thus if the bin width is *h*, and the mid-interval value is x_i, the interval has a range from x_i-*h*/2 to x_i+*h*/2. This assumption hides the within-interval variation in values which may create some errors in computations, especially if the class width are large. The so-called Sheppard's correction, named after its author William Sheppard (1897), is an adjustment to estimates of the variance when (Normally distributed) fixed width bins are used. Without correction the computations tend to over-estimate the variance since they effectively treat all values in a range as the same as the mid-value. Sheppard's correction to the variance is $-h^2/12$, an amount that is the variance of the Uniform distribution defined over an interval of width, *h*.

The table below provides details of a number of univariate classification schemes together with comments on their use. Such schemes are essentially a generalization of fixed-width binning. Many statistical software packages provide classification options of the types listed, although some (such as the box, Jenks and percentile methods) are only available in a limited number of software tools.

The scheme described in the table as Natural breaks or Jenks' method is an automated procedure utilizing the following algorithm:

Step 1: The user selects the attribute, x, to be classified and specifies the number of classes required, k

Step 2: A set of k-1 random or uniform values are generated in the range [min{x},max{x}]. These are used as initial class boundaries or 'cut points'

Step 3: The mean values for each initial class are computed and the sum of squared deviations of class members from the mean values is computed. The total sum of squared deviations (TSSD) is recorded

Step 4: Individual values in each class are then systematically assigned to adjacent classes by adjusting the class boundaries to see if the TSSD can be reduced. This is an iterative process, which ends when improvement in TSSD falls below a threshold level, i.e. when the within class variance is as small as possible and between class variance is as large as possible. True optimization is not assured. The entire process can be optionally repeated from Step 1 or 2 and TSSD values compared

Univariate binning/classification schemes

Classification scheme	Description/application
Unique values	Each value is treated separately — this is effectively a nominal data classification model
Manual classification	The analyst specifies the boundaries between classes/bins as a list, or specifies a lower bound and interval or lower and upper bound plus number of intervals required. This approach is widely used in statistical software packages
Equal interval	The attribute values are divided into n classes with each interval having the same width=range/n
Exponential interval	Intervals are selected so that the number of observations in each successive interval increases (or decreases) exponentially
Equal count or quantile	Intervals are selected so that the number of observations in each interval is the same. If each interval contains 25% of the observations the result is known as a quartile classification. Ideally the procedure should indicate the exact numbers assigned to each class, since they will rarely be exactly equal
Percentile	In the standard version equal percentages (percentiles) are included in each class, e.g. 20% in each class. In some implementation of percentile plots (specifically designed for exploratory data analysis, EDA) unequal numbers are assigned to provide classes that, for example, contain 6 intervals: <=1%, >1% to <10%, 10% to <50%, 50% to <90%, 90% to <99% and >=99%
Natural breaks/Jenks	Used within some software packages, these are forms of variance-minimization classification. Breaks are typically uneven, and are selected to separate values where large changes in value occur. May be significantly affected by the number of classes selected and tends to have unusual class boundaries. Typically the method applied is due to Jenks, as described in Jenks and Caspall (1971, [JEN1]), which in turn follows Fisher (1958, [FIS1]). Very useful for visualization work, but unsuitable for comparisons
Standard deviation (SD)	The mean and standard deviation of the data are calculated, and values classified according to their deviation from the mean (z-transform). The transformed values are then grouped into classes, usually at intervals of 1.0 or 0.5 standard deviations. Note that this often results in no central class, only classes either side of the mean and the number of classes is then even. SD classifications in which there is a central class (defined as the mean value +/-0.5SD) with additional classes at +/- 1SD intervals beyond this central class, are also used
Box	A variant of quartile classification designed to highlight outliers, due to Tukey (1977, Section 2C, [TUK1]). Typically six classes are defined, these being the 4 quartiles, plus two further classifications based on outliers. These outliers are defined as being data items (if any) that are more than 1.5 times the inter-quartile range (IQR) from the median. An even more restrictive set is defined by 3.0 times the IQR. A slightly different formulation is sometimes used to determine these box ends or hinge values

Supervised binning and classification

Some statistical software packages differentiate between *unsupervised* and *supervised* schemes. These terms have different meanings within different packages and application areas, which can be confusing. In broad terms an

unsupervised method utilizes the data directly, whereas a supervised method cross-refers the sample data to some other dataset that is already divided into a number of distinct classes or categories. It then uses this other dataset to guide (or supervise) the classification process.

In SPSS, for example, supervised (or *optimal*) binning refers to a procedure in which the source data is divided into bins using cut-points that seek to minimize the mix of a separate, but linked, nominal variable in each bin. For example, the variable to be binned might be household income in $000s p.a., and the supervisor or control variable might be the level of education achieved by the main earner of the household. The principal technique used, known as MDLP, starts by placing every (sorted) data item (observation) into a single large bin. The bin is then divided using cut-points, and the mix of the linked nominal variable in each bin is examined (using an Entropy or Diversity statistic). If every entry in the bin has the same linked nominal category then the Entropy measure will be 0, which is regarded as optimal with respect to the nominal variable. On the other hand if there is a large mix of nominal variables represented, of roughly equal numbers, the bin will have a higher Entropy score. The algorithm adjusts the cut points and increases the number of cut points (and hence bins) to achieve an improvement in the total Entropy of the binning process.

In remote-sensing applications (for example, multi-spectral satellite imagery) the task is to classify individual image pixels into groups, which may be pre-defined (e.g. land use categories, such as Forest, Grasslands, Buildings, Water etc) or derived from the data. Unsupervised classification in this instance refers to the use of wholly automated procedures, such as K-means clustering, in order to group similar pixels. Supervised classification refers to a multi-stage process, in which the dataset is compared to a reference dataset that has already been classified, and the similarity between pixels in the dataset to be classified and the reference set is used as a means for achieving the 'best' classification. Clearly procedures such as this, which arise in a number of disciplines, essentially belong in the realm of multivariate data classification, which may or may not use statistical techniques and measures as part of that process.

Scale and arrangement

In the preceding subsections we have seen that determining the ideal number and size of bins can be a quite complicated exercise. It was noted that with too many bins only frequencies of 1 and 0 would be recorded, whereas with very few bins, almost all the variation in the data would be hidden within the bin, or class, with little or no variation detectable between classes. This is often the exact opposite of the ideal classification or grouping schemes, where the aim is generally to minimize within-class variance as compared to between class variance — making sure that classes or groupings are as homogeneous as possible. Two additional, and somewhat unexpected factors, come into play when such groupings are made. These are known as the *statistical effect* and the *arrangement effect*.

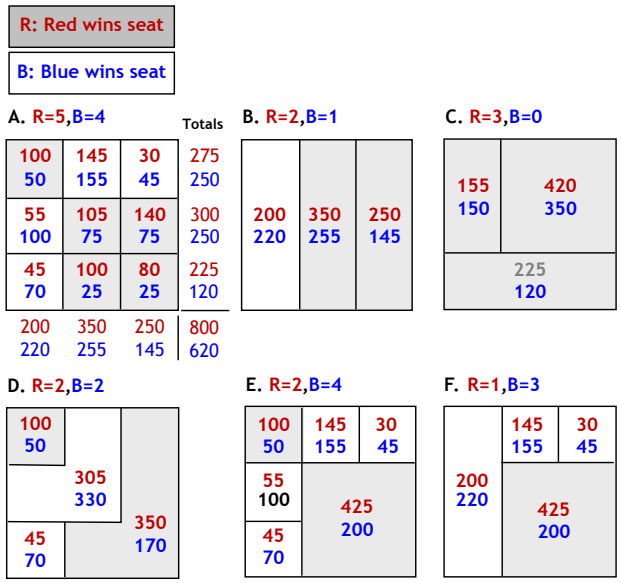
To understand the statistical effect (which is a scale or grouping effect) look at the regional employment statistics shown in the Table below (after de Smith *et al.* (2018, [DES1]). Areas A and B both contain a total of 100,000 people who are classified as either employed or not. In area A 10% of both Europeans and Asians are unemployed (i.e. equal proportions), and likewise in Area B we have equal proportions (this time 20% unemployed). So we expect that combining areas A and B will give us 200,000 people, with an equal proportion of Europeans and Asians unemployed (we would guess this to be 15%), but it is not the case — 13.6% of Europeans and 18.3% of Asians are seen to be unemployed! The reason for this unexpected result is that in Area A there are many more Europeans than Asians, so we are working from different total populations.

Regional employment data — grouping effects

	Employed (000s)	Unemployed (000s)	Total (000s) (Unemployed %)
Area A			
European	81	9	90 (10%)
Asian	9	1	10 (10%)
Total	90	10	100 (10%)
Area B			
European	40	10	50 (20%)
Asian	40	10	50 (20%)
Total	80	20	100 (20%)
Areas A and B			
European	121	19	140 (13.6%)
Asian	49	11	60 (18.3%)
Total	170	30	200 (15%)

There is a further, less well known problem, which has particular importance in the process of elections and census data collection but also has much wider implications. This is due to the way in which voting and census areas are defined. Their shape, and the way in which they are aggregated, affects the results and can even change which party is elected. The Grouping Data diagram below illustrates this issue for an idealized region consisting of 9 small voting districts. The individual zone, row, column and overall total number of voters are shown in diagram A, with a total of 1420 voters of whom roughly 56% (800) will vote for the Red party (R) and 44% (620) for the Blue party (B). With 9 voting districts we expect roughly 5 to be won by the Reds and 4 by the Blues, as is indeed the case in this example. However, if these zones are actually not the voting districts themselves, but combinations of the zones are used to define the voting areas, then the results may be quite different. As diagrams B to F show, with a voting system of “first past the post” (majority in a voting district wins the district) then we could have a result in which every district was won by the Reds (Case C), to one in which 75% of the districts were won by the Blues (Case F). So it is not just the process of grouping that generates confusing results, but also the pattern of grouping. We are rarely informed of the latter problem, although it is one that is of great interest to those responsible for defining and revising electoral and census district boundaries.

Grouping Data — Zone arrangement effects on voting results



This is not just a problem confined to voting patterns and census data. For example, suppose the information being gathered relates to the average levels of lead and zinc in the soil within each field. Samples based on different field boundaries would show that in some arrangements the average proportion of lead in the soil exceeded that of zinc, whilst other arrangements would show the opposite results.

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2.1 The Statistical Method

Many people would regard statistical analysis as a purely technical exercise involving the application of specialized data collection and analysis techniques, but this perception is both incorrect and misleading. Statistical problems should be viewed within the context of a broad methodological framework, and it is the specific nature of this framework that defines "The Statistical Method". Here we are using the terminology and interpretation of MacKay and Oldford (2000, [MAC1]). They carefully examined the nature of statistical analysis by discussing the problem of determining the speed of light, as conducted in the experiments of A A Michelson in 1879. Although they used research that involved a relatively complicated experiment as their example, the conclusions they draw are much more wide-reaching. Essentially they argue that statistical analysis must involve a broad perspective on the task under consideration, from the initial Problem definition stage (P), through Planning and Data collection stages (P,D) through to Analysis (A) and Conclusions (C). This is similar to the "statistical problem solving cycle" as described in the Probability & Statistics leaflet mentioned in our Suggested Reading section and elsewhere, but widens the scope of this methodology.

The elements of this methodological framework are shown in the PPDAC table below — each is discussed in detail in their paper. MacKay and Oldford note that very often the complexity of the analysis phase is greatly reduced if the totality of a problem is addressed in the manner described. As can be seen, the formal analysis stage comes well down the sequence of steps that are involved in producing good quality statistical research. Absolutely crucial to the entire process is the initial problem definition. Only once this is thoroughly understood by all interested parties can a plan for data collection be devised and the data obtained for subsequent analysis.

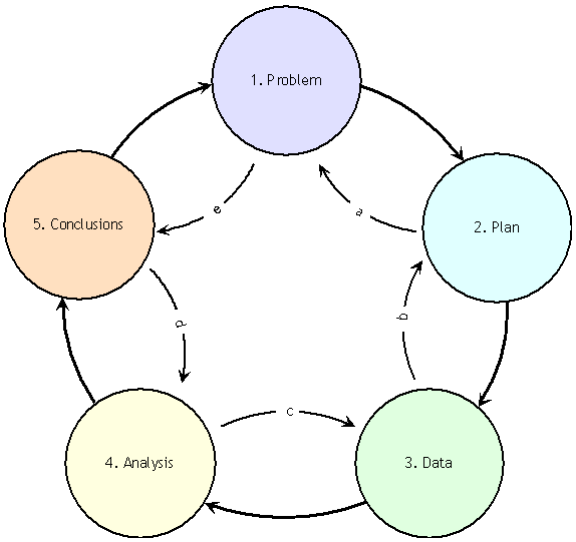
PPDAC: The Statistical Method, after MacKay and Oldford (2000)

	Details	Michelson experiment
Problem	Units & Target Population (Process) Response Variate(s) Explanatory Variates Population Attribute(s) Problem Aspect(s) — causative, descriptive, predictive	Unit: One (measured) light transmission. Population: all such transmissions Response variate: the speed of light in each measured transmission Explanatory variates: a large number of possible factors that might help explain variations in the measured data (e.g. method used, the measurement process) Population attributes: the average speed of light in a vacuum Problem aspect: descriptive (seeking an estimate of a specific value)
Plan	Study Population (Process) (Units, Variates, Attributes) Selecting the response variate(s) Dealing with explanatory variates Sampling Protocol Measuring processes Data Collection Protocol	Study population: The collection of units that could possibly be measured (known as the sampling frame in survey work). Michelson measured the speed of light in air, not in a vacuum — the difference between the study population and the true population is known as the *study error* Response variates: Michelson measured the speed of light indirectly, using distances, rotation speed (of a mirror), timing device (tuning forks) and temperature Explanatory variates: There may be a large number. Where possible Michelson tried to fix those factors he was aware of, and measure or vary others to check if they had an effect on his results

	Details	Michelson experiment
		Sampling protocol: The detailed procedure followed for sampling the data — in Michelson's case he made sets of measurements one hour after sunrise and one hour before sunset, on a series of days close to mid-summer. He made 1000 measurements, with some made by an independent observer Measuring processes: the equipment, people, and methods used — *measurement error* , which is the difference between the measured value and the true value, is incurred in this step of the procedure Data Collection Protocol: the management and administration (recording etc) of the entire data collection exercise — nowadays this would include data storage and processing considerations
Data	Execute the Plan and record all departures Data Monitoring Data Examination for internal consistency Data storage	Execution: Michelson did not record every result, but just the average values for blocks of 10 measurements Data monitoring: Tracking data as they are obtained helps identify patterns, temporal drift, outliers etc. Michelson did not explicitly do this Data examination: The internal consistency of the data should be checked, for unexpected features (each using EDA techniques), but Michelson did not appear to do this Data storage: simple tabulated results on paper in this instance
Analysis	Data Summary numerical and graphical Model construction build, fit, criticize cycle Formal analysis	In Michelson's case he summarized his data in tables and computed the average of his 100 measured velocities in air, and then corrected for the deflection effect that air would have on his results, making a small adjustment for temperature variations in each case. Formal analysis was limited to analyzing possible source of error and their maximum impact on the results, in order to obtain an estimate of the velocity of light in a vacuum, +/- the estimated errors
Conclusion	Synthesis plain language, effective presentation graphics Limitations of study discussion of potential errors	Michelson presented his central finding and provided a full discussion as to possible sources of error and why many factors could be ignored due to the manner in which the plan was made and executed. Despite this, the true value for the speed of light is actually outside the limits of his estimates at the time, even though his mean result was within 0.05% of the correct figure, hence he slightly underestimated the size of the errors affecting his result

The PPDAC summary table suggests a relatively linear flow from problem definition through to conclusions — this is typically not the case. It is often better to see the process as cyclical, with a series of feedback loops. A summary of a revised PPDAC approach is shown in the diagram below. As can be seen, although the clockwise sequence (1→5) applies as the principal flow, each stage may and often will feed back to the previous stage. In addition, it may well be beneficial to examine the process in the reverse direction, starting with Problem definition and then examining expectations as to the format and structure of the Conclusions (without pre-judging the outcomes!). This procedure then continues, step-by-step, in an anti-clockwise manner (e→a) determining the implications of these expectations for each stage of the process.

PPDAC as an iterative process



We now expand our discussion by examining the components this revised model in a little more detail:

Problem: Understanding and defining the problem to be studied is often a substantial part of the overall analytical process — clarity at the start is obviously a key factor in determining whether a programme of analysis is a success or a failure. Success here is defined in terms of outcomes (or objectives) rather than methods. And outcomes are typically judged and evaluated by third parties — customers, supervisors, employers — so their active involvement in problem specification and sometimes throughout the entire process is essential. Breaking problems down into key components, and simplifying problems to focus on their essential and most important and relevant components, are often very effective first steps. This not only helps identify many of the issues to be addressed, likely data requirements, tools and procedures, but also can be used within the iterative process of clarifying the customer's requirements and expectations. Problems that involve a large number of key components tend to be more complex and take more time than problems which involve a more limited set. This is fairly obvious, but perhaps less obvious is the need to examine the interactions and dependencies between these key components. The greater the number of such interactions and dependencies the more complex the problem will be to address, and as the numbers increase complexity tends to grow exponentially. Analysis of existing information, traditionally described as "desk research", is an essential part of this process and far more straightforward now with the advantage of online/Internet-based resources. Obtaining relevant information from the client/sponsor (if any), interested third parties, information gatekeepers and any regulatory authorities, forms a further and fundamental aspect to problem formulation and specification. Box *et al*. (2005, p13, [BOX1]) suggest a series of questions that should be asked, particularly in the context of conducting experiments or trials, which we list below with minor alterations from their original. As can be seen, the questions echo many of the issues we raise above:

- what is the objective of this investigation?
- who is responsible?
- I am going to describe your problem — is my description correct?

- do you have any past data? and if so, how were these data collected/in what order/on what days/by whom/how?
- do you have any other data like these?
- how does the equipment work/what does it look like/can I see it?
- are there existing sampling, measurement and adjustment protocols?

Plan: Having agreed on the problem definition the next stage is to formulate an approach that has the best possible chance of addressing the problem and achieving answers (outcomes) that meet expectations. Although the PLAN phase is next in the sequence, the iterative nature of the PPDAC process emphasizes the need to define and then re-visit each component. Thus whilst an outline project plan would be defined at this stage, one would have to consider each of the subsequent stages (DATA, ANALYSIS, CONCLUSIONS) before firming up on the detail of the plan. With projects that are more experimental in nature, drawing up the main elements of the PLAN takes place at this stage. With projects for which pre-existing datasets and analysis tools are expected to be used, the PLAN stage is much more an integrated part of the whole PPDAC exercise. The output of the PLAN stage is often formulated as a detailed project plan, with allocation of tasks, resources, times, analysis of critical path(s) and activities, and estimated costs of data, equipment, software tools, manpower, services etc. Frequently project plans are produced with the aid of formal tools, which may be paper-based or software assisted. In many instances this will involve determining all the major tasks or task blocks that need to be carried out, identifying the interconnections between these building blocks (and their sequencing), and then examining how each task block is broken down into sub-elements. This process then translates into an initial programme of work once estimated timings and resources are included, which can then be modified and fine-tuned as an improved understanding of the project is developed. In some instances this will be part of the Planning process itself, where a formal functional specification and/or pilot project forms part of the overall plan. As with other parts of the PPDAC process, the PLAN stage is not a one-shot static component, but typically includes a process of monitoring and re-evaluation of the plan, such that issues of timeliness, budget, resourcing and quality can be monitored and reported in a well-defined manner. The approach adopted involves consideration of many issues, including:

- the nature of the problem and project — is it purely investigative, or a formal research exercise; is it essentially descriptive, including identification of structures and relationships, or more concerned with processes, in which clearer understanding of causes and effects may be required, especially if predictive models are to be developed and/or prescriptive measures are anticipated as an output?
- does it require commercial costings and/or cost-benefit analysis?
- are particular decision-support tools and procedures needed?
- what level of public involvement and public awareness is involved, if any?
- what particular operational needs and conditions are associated with the exercise?
- what time is available to conduct the research and are there any critical (final or intermediate) deadlines?
- what funds and other resources are available?
- is the project considered technically feasible, what assessable risk is there of failure and how is this affected by problem complexity?
- what are the client (commercial, governmental, academic, personal) expectations?

- are there specifications, standards, quality parameters and/or procedures that must be used (for example to comply with national guidelines)?
- how does the research relate to other studies on the same or similar problems?
- what data components are needed and how will they be obtained (existing sources, collected datasets)?
- are the data to be studied (units) to be selected from the target population, or will the sample be distinct in some way and applied to the population subsequently (in which case, as discussed earlier, one must consider not just *sampling error* but *study error* also)?

When deciding upon the design approach and analytical methods/tools it is often important to identify any relevant available datasets, examine their quality, strengths and weaknesses, and carry out exploratory work on subsets or samples in order to clarify the kind of approach that will be both practical and effective. There will always be unknowns at this stage, but the aim should be to minimize these at the earliest opportunity, if necessary by working through the entire process, up to and including drafting the presentation of results based on sample, hypothetical or simulated data.

Data: In research projects that involve experiments, the data are collected within the context of well-defined and (in general) tightly controlled circumstances, with the response and explanatory variates being clearly included in the design of the experiment. In many other instances data is obtained from direct or indirect observation of variates that do not form part of any controlled experiment. And in survey research, although there will be a carefully constructed sample design, the level of direct control over variates is typically very limited. Key datasets are also often provided by or acquired from third parties rather than being produced as part of the research. Analysis is often of these pre-existing datasets, so understanding their quality and provenance is extremely important. It also means that in many instances this phase of the PPDAC process involves selection of one or more existing datasets from those available. In practice not all such datasets will have the same quality, cost, licensing arrangements, availability, completeness, format, timeliness and detail. Compromises have to be made in most instances, with the over-riding guideline being fitness for purpose. If the datasets available are unsuitable for addressing the problem in a satisfactory manner, even if these are the only data that one has to work with, then the problem should either not be tackled or must be re-specified in such a way as to ensure it is possible to provide an acceptable process of analysis leading to worthwhile outcomes. A major issue related to data sourcing is the question of the compatibility of different data sets: in formats and encoding; in temporal, geographic and thematic coverage; in quality and completeness. In general datasets from different sources and/or times will not match precisely, so resolution of mismatches can become a major task in the data phase of any project. And as part of this process the issue of how and where to store the data arises, which again warrants early consideration, not merely to ensure consistency and retrievability but also for convenient analysis and reporting. Almost by definition no dataset is perfect. All may contain errors, missing values, have a finite resolution, include distortions as a result modeling the real world with discrete mathematical forms, incorporate measurement errors and uncertainties, and may exhibit deliberate or designed adjustment of data (e.g. for privacy reasons, as part of aggregation procedures).

Analysis: The Analysis phase can be seen as a multi-part exercise. It commences with the review of data collected and the manipulation of the many inputs to produce consistent and usable data. Exploratory data analysis (EDA), including the production of simple data summaries, tabulations and graphs is typically the first stage of any such analysis. The impact on research of exceptions — rare events, outliers, extreme values, unusual clusters — is extremely important. Exploratory methods, such as examining individual cases and producing box-plots, help to determine whether these observations are valid and important, or require removal from the study set. This phase

then extends into more formal study in order to identify patterns of various kinds that help the researcher to develop new ideas and hypotheses regarding form and process. And this in turn may lead on to the use or development of one or more models within a formal build-fit-criticize cycle. Crawley (2007, p339, [CRA1]) provides the following extremely sound advice regarding model selection (echoing a quote attributed to George Box):

> *"It is as well to remember the following truths about models: all models are wrong; some models are better than others* [Box said *more useful*]*; the correct model can never be known with certainty; and the simpler a model the better it is"!*

Finally the output of the models and analysis is examined, and where necessary the dataset and data gathering plan is re-visited, working back up the PPDAC model chain, prior to moving on to producing the output from the project and delivering this in the Conclusion stage. The application of a single analytical technique or software tool is often to be avoided unless one is extremely confident of the outcome, or it is the analytical technique or approach itself that is the subject of investigation, or this approach or toolset has been specifically approved for use in such cases. If analysis is not limited to single approaches, and a series of outputs, visualizations, techniques and tests all suggest a similar outcome then confidence in the findings tends to be greatly increased. If such techniques suggest different outcomes the analyst is encouraged to explain the differences, by re-examining the design, the data and/or the analytical techniques and tools applied. Ultimately the original problem definition may have to be reviewed.

Conclusions: The last stage of the PPDAC process is that of reaching conclusions based upon the analyses conducted, and communicating these to others. Note that implementation of findings (e.g. actually proceeding with building a bypass, designating an area as unfit for habitation, or implementing a vaccination programme) does not form part of this model process, but lies beyond its confines.

> *"The purpose of the Conclusion stage is to report the results of the study in the language of the Problem. Concise numerical summaries and presentation graphics* [*tabulations, visualizations*] *should be used to clarify the discussion. Statistical jargon should be avoided. As well, the Conclusion provides an opportunity to discuss the strengths and weaknesses of the Plan, Data and Analysis especially in regards to possible errors that may have arisen" Mackay and Oldford (2000)*

For many problems this summary is sufficient. For others the conclusions stage will be the start of additional work: re-visiting the problem and iterating the entire process or parts of the process; a new project; implementing proposals; and/or wider consultation. In Michelson's case, he was aware of several imperfections in his research, and in fact spent the rest of his life conducting a series of further experiments in order to progressively improve the accuracy of his estimate of the true speed of light. A full discussion of this revised PPDAC model in the context of spatial analysis is provided in the "Chapter 3: Spatial analysis and the PPDAC model" of de Smith *et al.*, 2018 [DES1] which is available online.

References

[BOX1] Box G E P,Hunter J S, Hunter W G (1978, 2005) Statistics for Experimenters: An Introduction to Design, Data Analysis and Model Building. J Wiley & Sons, New York. J Wiley & Sons, New York. The second, extended edition was published in 2005

[CRA1] Crawley M J (2007) The R Book. J Wiley & Son, Chichester, UK, 2nd ed 2015

[DES1] de Smith M J, Goodchild M F, Longley P A and Colleagues (2018) Geospatial Analysis: A Comprehensive Guide to Principles, Techniques and Software Tools. 6th edition, The Winchelsea Press. Available with public access from: http://www.spatialanalysisonline.com/

[MAC1] MacKay R J, Oldford R W (2000) Scientific Method, Statistical Method and the Speed of Light. Statist. Sci., 15, 3, 254-278. Available from: https://projecteuclid.org/euclid.ss/1009212817

Wikipedia, Speed of Light article: http://en.wikipedia.org/wiki/Speed_of_light

2.2 Misuse, Misinterpretation and Bias

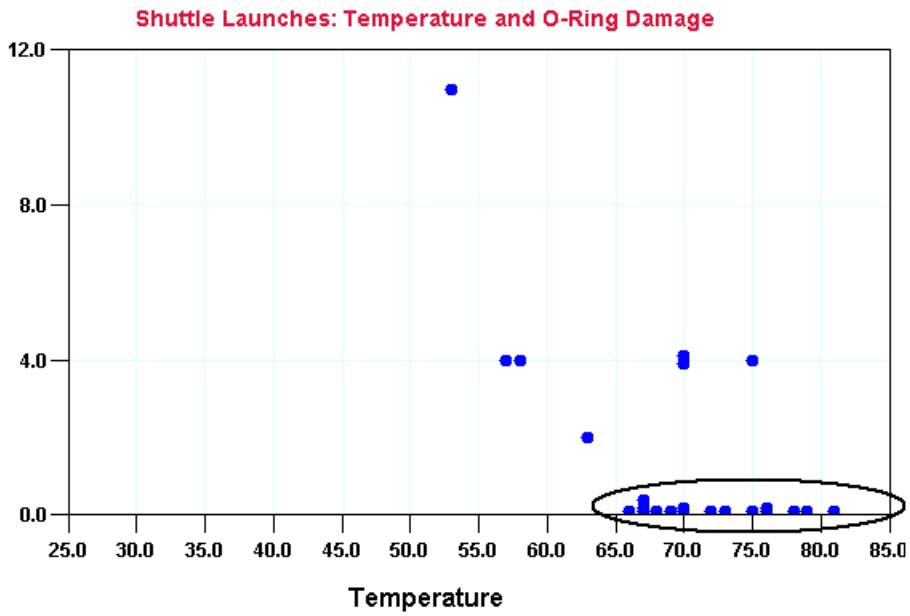
A great deal has been written about the misuse of statistics by pressure groups and politicians, by pollsters and advertising campaigns, by the broadcast media (newspapers, magazines, television, and now the Internet), and even misuse by statisticians and scientists. In some instances the misuse has been simply lack of awareness of the kinds of problems that may be encountered, in others carelessness or lack of caution and review, whilst on occasion this misuse is deliberate. One reason for this has been the growth of so-called *evidence-based* policy making — using research results to guide and justify political, economic and social decision-making. Whilst carefully designed, peer-reviewed and repeatable research does provide a strong foundation for decision-making, weak research or selective presentation of results can have profoundly damaging consequences. In this section we provide guidance on the kinds of problems that may be encountered, and comment on how some of these can be avoided or minimized. The main categories of misuse can be summarized as:

- inadequate or unrepresentative data
- misleading visualization of results
- inadequate reasoning on the basis of results
- deliberate falsification of data

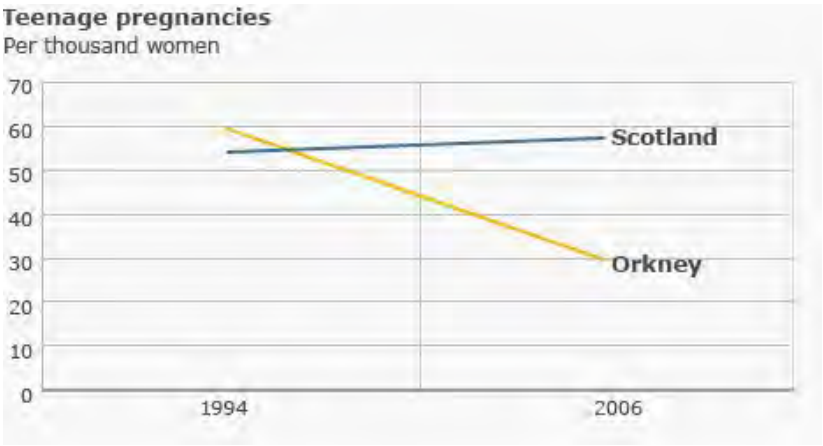
In the subsections of this topic we discuss each of these categories in turn.

Where data is obtained as the result of some form of trial, experiment or survey, careful design can help avoid many (but not all) of the problems identified in the first category (see also Design of Experiments and Bias). This is of particular importance in medical research, and for this reason we have included a separate subsection focusing on this particular application area and the kinds of problems and issues that are encountered.

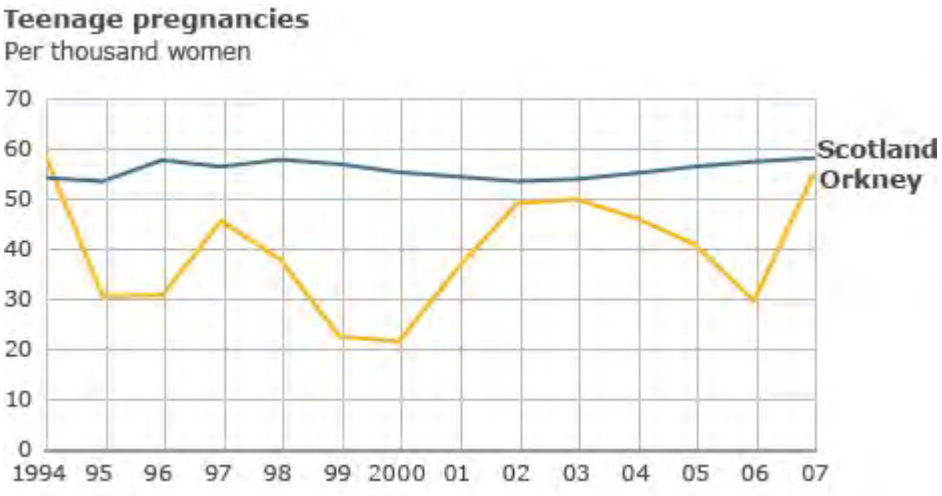
A simple example, which occurs only too frequently, is the presentation and interpretation of data where some data items are omitted. A much reported example of this concerned the analysis of the failure of O-rings on the US space shuttle in 1986. NASA staff and their contractors examined the pattern of failures of O-rings during launches against temperature just prior to the ill-fated shuttle launch on January 28 1986. They concluded that the data showed no apparent relationship between the number of failures and temperature, but as we now know, the low temperature overnight did result in a failure of these components (see graph below) with catastrophic results. What the analysts failed to consider were all those launches that had 0 failures. All the launches with no failures occurred when the ambient temperature at the launch site was much higher, as highlighted in the diagram (see also, the Space Shuttle dataset and example in the R library, vcd).



In a rather different context highlighted in Jan 2010 by BBC journalist Michael Blastland (see also, our Recommended Reading topic, [BLA1]). Reports of declining teenage pregnancy rates in Orkney off the north coast of Scotland, were shown to be highly misleading. Blastland showed two graphs. The first appears to show a halving of the teenage pregnancy rate between 1994 and 2006, following an intensive programme of education and support:



However, the reports omitted data for the intervening years, and as we know from stock market and many other types of data, rates of change depend very heavily on your start and end date. The data in this case is actually quite cyclical, and choosing 2006 rather than, say 2007, provides a completely misleading picture, as the graph below demonstrates.



In many instances misuse is not deliberate, but leads to biased results and conclusions that cannot be relied upon and the consequences can be serious.

Our final example concerns the question of independent sampling. On 2nd February 2010 a UK national newspaper, the Daily Mail, reported the story of a woman who had bought a box of 6 eggs and found that every one contained a double-yolk. They argued that because roughly 1 egg in a thousand has a double yolk, the chances of having a box with every one being double-yolks was one in a quintillion (1 in 10^{18}). It was clearly a crazy statement that assumed the occurrence of multiple yolks in a box of eggs represented a set of independent events, and that it was therefore valid to multiply 1:1000 x 1:1000 etc. 6 times. In fact the events are in no way independent, for a whole variety of reasons. One respondent to a discussion about this example pointed out that most eggs are boxed in large sorting and packing warehouses, and in some cases eggs are checked against a strong light source to see if they contain a double yolk. If they do, they are put to one side and the staff often take these home for their own use, but if there are too many they are simply boxed up, resulting in boxes of double-yolk eggs.

Inadequate or unrepresentative data

This is probably the most common reason for 'statistics' and statistical analysis falling short of acceptable standards. Problems typically relate to inadequacies in sampling, i.e. in the initial design of the data collection, selection or extraction process. This results in the sample, from which inferences about the population are made, being biased or simply inadequate. The following list includes some of the main situations which lead to such problems:

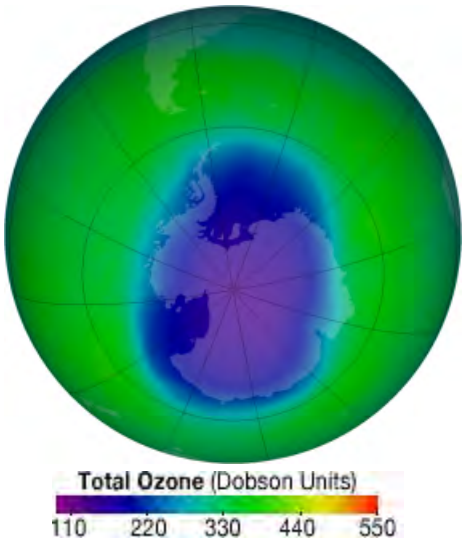
- **datasets and sample sizes** — there are many situations where the dataset or sample size analyzed is simply too small to address the questions being posed, or is not large enough for use with the proposed statistical technique, or is used in a misleading fashion. Smaller sample sizes are also more prone to bias from missing data and non-responses in surveys and similar research exercises. For example, when examining the incidence of particular diseases recorded in different census districts (or hospital catchment areas etc) we might find that for some diseases recorded cases were quite low in rural districts (<10), but were much higher in urban districts (>100). Does this mean the disease is more likely to occur amongst urban dwellers? Not necessarily, as there are

more urban dwellers. To remove the effect of differences in the *population-at-risk* we might decide to compute the incidence (or *rate*) of the disease per 1000 population in each district (perhaps stratified by age and sex). Because of the relatively low population-at-risk in the rural area this might then show the risk appears much higher in the rural areas. Is the risk really higher or is the result a reflection of the relatively small numbers reported? Is reporting of cases for this disease the same in rural and urban areas, or is there some differential in recording perhaps due to differences in the quality of health care available or for social reasons? For a rare disease, a reported 25% increase year-on-year in the incidence of a particular type of cancer in the rural district might simply be the result of an increase of a single new reported case. It is also important to be aware that small samples tend to be much more variable in *relative* terms than large samples. This can result in errors in reasoning, as we discuss later in this section (see also: Sampling and sample size). Large sample sizes are also no guarantee of the quality or lack of bias in the data. One very early failure of a large dataset was when the US Literary Digest's postal poll regarding the US presidential election in 1936 received roughly 2.4 million returns. With the aim of achieving as large a sample as possible, the magazine sought datasets that contained the names and addresses of millions of adults, these primarily comprised vehicle registration lists and telephone directories. In total, over 10 million letters were posted. However, despite receiving an impressive number of responses, the poll incorrectly predicted that Landon would beat Roosevelt. Their data sources are now understood to have produced biased samples that were likely to be of a higher socio-economic status. The rates of both automobile and telephone ownership were much lower amongst poorer adults at the time.

- **clustered sampling** — this issue relates to the collection of data in a manner that is known in advance to be biased, but is not subsequently adjusted for this bias. Examples include the deliberate decision to over-sample minority social groups because of expected lower response rates or due to a need to focus on some characteristic of these groups which is of particular interest — see, for example, the discussion of this issue by Brogan (1998, [BRO1]). A second example applies where the only available data is known to be clustered (in space and/or time) — for example, in order to obtain estimates of the levels of trace elements in groundwater it is often only possible to take samples from existing wells and river courses, which are often spatially clustered. If the samples taken are not subsequently weight-adjusted (or *de-clustered*) results may be biased because some groups or areas are sampled more than others
- **self-selection and pre-screening** — this is a widespread group of problems in sampling and the subsequent reporting of events. Surveys that invite respondents to participate rather than randomly selecting individuals and ensuring that the resulting survey sample is truly representative are especially common. For example, surveys that rely on opting in, such as those placed in magazines, or via the Internet, provide a set of data from those who read the publication or view the Internet site, which is a first category of selection, and from this set the individuals who choose to respond are then self-selecting. This group may represent those with a particular viewpoint, those with strong views (so greater polarization of responses) or simply those who have the time and inclination to respond. Likewise, a survey on lifestyle in the population at large that advertises for participants in a range of lifestyle magazines, or in fitness studios and sports clubs, is likely to result in a significantly biased sample of respondents
- **exclusions** — the process of research design and/or sampling may inadvertently or deliberately exclude certain groups or datasets. An example is the use of telephone interviewing, which effectively pre-selects respondents by telephone ownership. If the proportion of exclusions is very small (e.g. in this example, the current proportion of people with telephones in a given country may be very high) this may not be a significant issue. A different category of exclusion is prevalent where some data is easier to collect than others. For example, suppose one wishes to obtain samples of bacteria in the soil of a study region. Areas which are very inaccessible may be under-sampled or omitted altogether whilst other areas may be over-sampled. In a different context,

surveys of individuals may find that obtaining an ethnically representative sample is very difficult, perhaps for social or language reasons, resulting in under-representation or exclusion of certain groups — groups such as the disabled or very young or very old are often inadvertently excluded from samples for this reason. Limitations of time and/or budget are often factors that constrain the extent and quality of data collection and hence relevant and important data may be excluded for reasons of necessity or expediency. Data may also be deliberately or inadvertently excluded as being probably an error or outlier. In May 1985 the existence of the huge 'ozone hole' over the Antarctic (depleted levels of ozone at high altitudes) was documented by research published in Nature magazine: *"NASA soon discovered that the spring-time 'ozone hole' had been covered up by a computer-program designed to discard sudden, large drops in ozone concentrations as 'errors'. The Nimbus-7 data was rerun without the filter-program and evidence of the Ozone-hole was seen as far back as 1976."* (source: NASA)

The ozone hole over Antarctica, November 2009



Darker/Blue zone indicates ozone level <220 Dobson units; source: NASA http://ozonewatch.gsfc.nasa.gov

- **exclusions, continued** — in an extremely thorough UK study of cancer incidence over 30 years amongst children in the vicinity of high-voltage overhead transmission lines, the authors, Draper *et al.* (2005, [DRA1]), appeared to cover every possible factor and issue. However, examining their research unstated questions (exclusions from the research) soon become apparent: no active participation from patients or their families was involved, and homes were not visited to measure actual levels of Electro-Magnetic (EM) radiation — this raises the question 'is home address at birth (which the authors used) an appropriate and sufficiently accurate measure'? (the authors did not include duration at the address, or where the children went to nursery etc); is vertical as well as horizontal proximity to high voltage lines of importance? (they only considered horizontal distance); is proximity to pylons carrying insulators and junction equipment rather than just the lines an important factor? (they omitted this issue altogether)
- **pre-conceptions** — researchers in scientific and social research frequently have a particular research focus, experience and possibly current norms or paradigms of their discipline or society at large. This may result in inadvertent use of techniques or survey questions that influence the outcome of the research. A common

problem is the wording of questions may lead the respondent to respond in a particular manner. Pre-conceptions may easily also lead to weak or incorrect reasoning from the data to conclusions

- **data trawling** — with large multi-variate datasets there is a high probability that statistically significant findings can be discovered somewhere in the data — brute-force processing of datasets looking for significant results that relate to a particular area of research interest, with or without explicit pre-conceptions, will often succeed but may well be entirely spurious. Techniques such as data-mining, cluster-hunting and factor analysis may all be 'misused' in this way
- **temporal or spatial effects** — the temporal or spatial sequence or arrangement of samples may be of critical importance, for many reasons. Examples of temporal effects include: dependence of test results on previous tests (e.g. in wine tasting); the temporal context of research — responses to questions on a particular topic may be very different if that topic has had a very high profile in the news in the immediate past (e.g. personal safety, terrorism, heart disease from too much salt in the diet, attitudes to eating Beef following the BSE/vCJD scare etc.) — this affects both the nature and the absolute levels (assigned values) of responses; temporal effects can also be observed in data collected as a sequence using research staff whose accuracy and attention diminish over time (for example in repeated recording of counts in microscopy; or repeated digitization of data points, of repeated asking of questions to interviewees). Examples of spatial effects include: location dependence (for example social groupings in specific areas, types of building, membership of organizations etc); local correlation of results due to water, materials or other flows (e.g. contaminant levels in soil samples at various locations may be related to each other due to groundwater or other localized effects). Missing data (unsampled or lost data) in the temporal and spatial domains are also very common, especially with automated monitoring equipment that may fail for brief or extended period (e.g. the NASA satellite monitoring data for high-atmosphere ozone levels from 1978 onwards was not available for much of 1995 due to technical problems)
- **over- and under-scoring** — the responses individuals provide to questions or tasks often show a distinct bias. When asked to state how confident the respondent is in the answer they have given, almost always the confidence level is over-stated, typically by 10-20% based on the relative frequency of correct responses. In some cultures diligence in completing surveys is taken much more seriously than in others. In one instance the present author achieved a greater than 100% response rate to a one page questionnaire asking respondents to list their activities on a given day — in principle impossible, but in fact many respondents photocopied the questionnaire and completed multiple sheets, even though this was not requested. Such response patterns are the exception — under-reporting is far more prevalent. In some instances the errors can be detected, for example by independent measurement or using a separate survey methodology. For example, when asked to record each telephone call made and its duration, respondents typically under-record the number of calls but over-score the duration, often rounding up to 1- or 5-minute multiples. The product of this particular over-scoring of duration and under-scoring of instances is generally close to the call hours (traffic, or Erlangs) measured using automatic call monitoring equipment, so the effect in terms of traffic estimation tends to cancel out in this case
- **deliberate bias** — by judicious selection, combination, arrangement and/or reporting of data (which may have been extremely carefully collected) is an important and serious area of misuse. Examples include: deliberate omission of data that does not fit the preconceptions of the researcher, or the conclusions they are seeking; omission or adjustment of data (this may be acceptable practice in some instances, but should always be made explicit — for example, exclusion of outliers on the grounds that they appear to be recording errors). Examples in the temporal domain include reporting results for selected time periods, or against selected 'base years' to suggest large changes that may not be of any significance; examples in the spatial domain include re-arranging the set of zones for which reporting is being carried out to increase or decrease a particular level of a variable

or correlation — this has a particular historical context in politics, where the practice has become known as Gerrymandering, and in spatial analysis, where the question has been studied in detail and is known as the MAUP problem (see further: Statistics and Statistical Analysis)

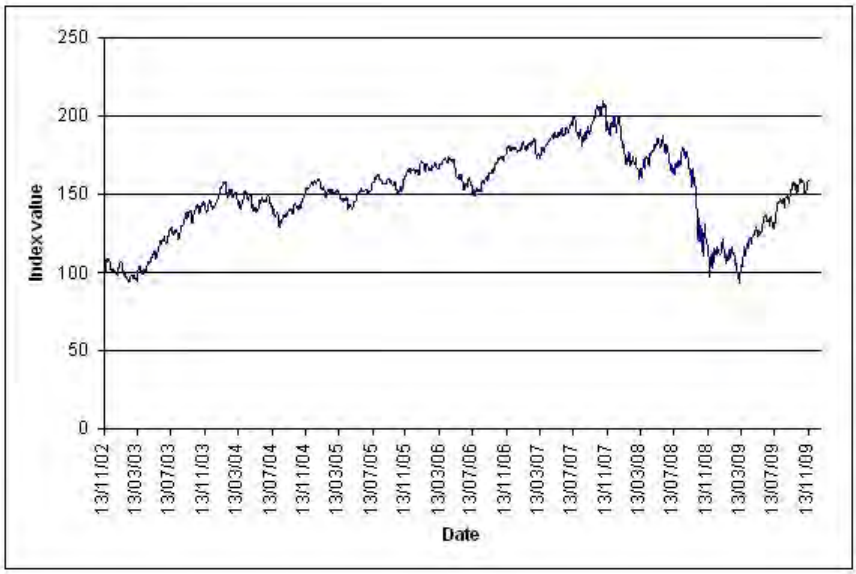
Misleading visualization of results

To be meaningful a statistical graph or chart should indicate:

- what the scales are
- whether it starts at zero or some other value, and
- how it was calculated, in particular exactly what dataset and time period it is based upon

Without all of these elements the information presented should be viewed with caution (as is clear from our example of teenage pregnancy data in the previous section). Line graphs and histograms that simply show the neighborhood of the top of the diagram are, in most instances, misleading. Similar issues may arise if not all intermediate datapoints are plotted, or if data prior to or after the plotted sequence is not shown but would place the information in a more meaningful and complete context. Likewise, charts that show the change over time from some base date, must be viewed with caution — changing the base date may significantly alter the values, even if the broad pattern remains unchanged. The chart below shows the daily closing price of the NASDAQ 100 stock index from a base value of 100 in late 2002 to late 2009 (7 years data). Clearly some variation is not visible, whilst within-day fluctuations are not reported. Non-trading days are omitted, which is entirely valid, so the *x*-axis is actually not strictly a time scale but is actually an event sequence, so could easily be numbered 1,2,3... etc without much loss of interpretation assuming the start date was known. With a base index of 100 the graph shows a 50% rise over 7 years, but clearly within any given window there are many movements up and down. A 5 year window (base re-computed as 100 for 5 years data to late 2009) would suggest no change.

NASDAQ 100 stock index history (2002-2009)



Similar issues apply to all forms of visualization, indeed increasingly so as automatic creation of static and dynamic charts, diagrams, classified maps and 3D representations become increasingly widespread. Of particular concern is the issue of comparability. Visualizations that may be used to compare data from different sources, datasets, times and/or locations, must be directly comparable in both design and scaling, otherwise comparison is almost impossible. This applies to both distinct visualizations and those that show super-imposed data. For further discussion of visualization issue, please see the Graphics and Visualization topic.

Inadequate reasoning

Drawing conclusions from research findings is always a complex process, often subject to debate. The confidence that can be placed on conclusions will depend, in part, on the nature and quality of the data collected and analyzed, and the quality of the reasoning applied to the interpretation of the findings. Certain types of reasoning may appear entirely plausible but on closer examination can be seen as fundamentally flawed. The list below provides a number of commonly encountered problems of this type.

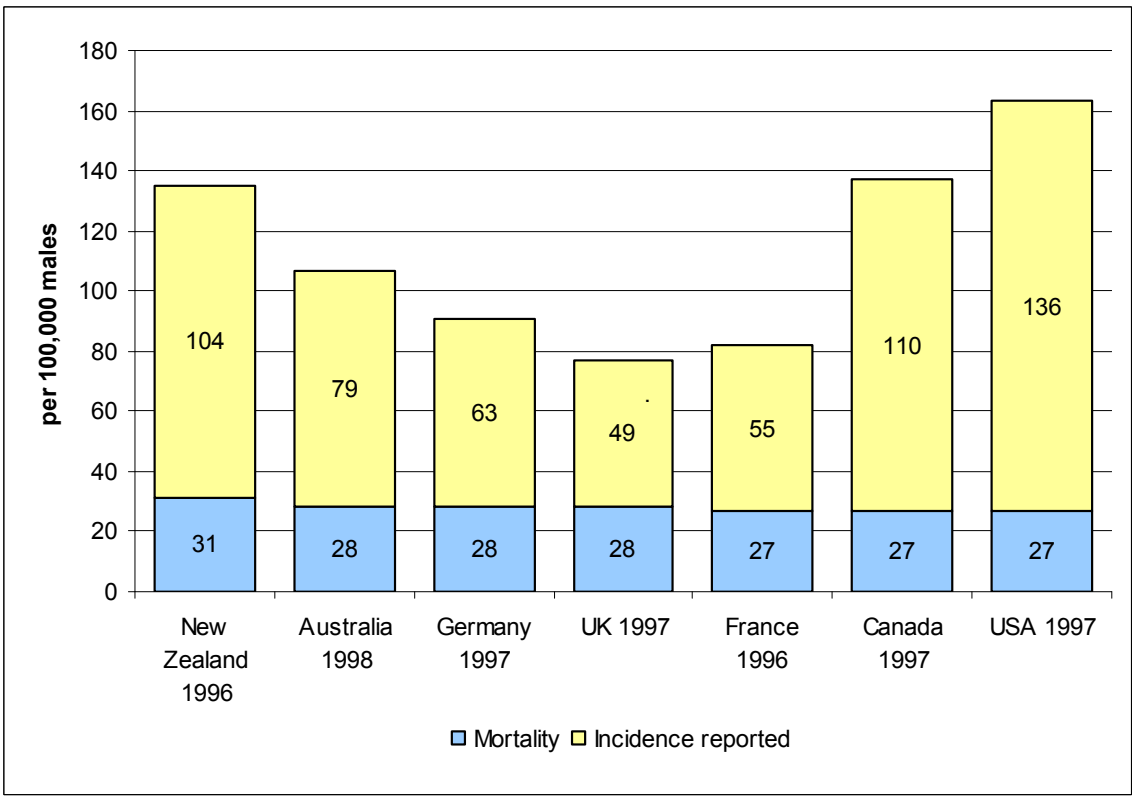
- **Correlation versus causation** — it is extremely easy to assume that because there is a close (perhaps highly significant) relationship between two variables, that one *causes* the other. This may occur in many ways and can be quite subtle (obvious examples are much easier to spot). Take the following example: "Girls at single sex schools do better than girls in mixed schools, therefore single-sex schools are better for girls". Based on test results in the UK and in a number of other countries the first part of this statement is well documented, but is the second part, which is a conclusion implying causality, actually correct? Without closer examination it is difficult to know. Further research shows that other factors are at work: (i) single-sex girls schools are often fee-paying, and wealthier families tend to have children who achieve higher academic results than less well-off families (there may be several reasons for this observed finding); (ii) single-sex girls schools are often selective, requiring entrance exams and/or interviews, thus filtering out groups who might under-perform or otherwise affect the academic results achieved; (iii) fee-paying schools often have longer days and more intensive teaching than non-fee paying schools. Put more formally, we can say that the fact that X and Y are correlated, or vary together, tells us relatively little about the causal relationship between X and Y. So, if X and Y vary together in some consistent manner, it might be that X causes Y, or Y causes X or that some set of third variables, Z are involved, such that Z causes X and Z causes Y so that the correlation of X and Y is simply due to their relationship to Z. Establishing causal relationships beyond doubt can be extremely difficult, but is often made easier by careful experimental design, thorough analysis of related factors, and repeated, independent, randomized trials. Recent examples of this kind of inadequate cause-effect reasoning include: the observation that breast cancer rates are higher in countries that have a high fat content in their diet, and then suggesting that women who eat more fat in their diet are more likely to suffer from breast cancer; or that crime rates are higher in areas of high unemployment, and then stating that it is the unemployed who are responsible for most crimes. The inferences drawn may be valid, and such observations can provide very useful pointers for research, but the data only provides very tenuous support for the claims made. Sets of "guidelines" and a number of special statistical methods have been developed over the last few decades that attempt to provide a formal framework for developing models that seek to pinpoint causal relationships. The formal methods include Rubin Causal Modeling (RCM), Structural Equation Modeling (SEM), and various forms of path modeling. These issues are discussed further in the section below on statistics in medical research
- **Misunderstanding of the nature of randomness and chance** — there are a number of ways in which natural randomness of events can be misunderstood, leading to incorrect judgments or conclusions. A simple example is misjudging the effect of sample size. Suppose that a large hospital has 40 births per day on average, with 50% of

these being boys. A smaller hospital nearby has 10 births/day, also 50% being boys on average. On some days the proportion of boys will be higher, on others lower. Which hospital would you expect to have the most days in a year with at least 60% of births being boys? The answer is the smaller hospital, because its records will exhibit inherently more variability — a change from 5 boys to 6 is sufficient to raise the proportion to 60%, whereas the larger hospital would need to have at least 4 more boys than girls born to result in a 60%+ result, which is less likely to occur. A second example is the assumption that in a particular sequence of chance or random events in the past is a guide to events in the future — for instance, the probability that an unbiased coin toss will result in heads is not affected by the fact that perhaps the previous 10 times it has shown up tails. It is probable but not certain that sooner or later the tossed coin will come down heads, but that probability does not change from toss to toss. A similar, and perhaps more disturbing example, is the so-called prosecutor's fallacy. In this instance a prosecutor calls an expert witness who states that a piece of evidence (for example, an extremely rare blood group or condition) provides a link to the accused which would only occur one time in a million. The prosecutor then claims on the basis of this opinion that there is only one chance in a million that the accused is innocent. But we do not know that the accused is guilty (a presumption of guilt is not a satisfactory starting point). If we assume the accused is innocent, how many other people in the population might also demonstrate such a link? The person accused might be guilty, but additional evidence would be needed before reaching such a conclusion. Readers interested in this particular field should read the free Statistics Guide for Lawyers (PDF) available on the RSS website. This is a highly recommended resource for both lawyers and non-lawyers alike

- **Ecological fallacy** — this fallacy involves ascribing characteristics to members of a group when only the overall group characteristics are known (special statistical techniques have been devised to address certain problems of this type, for example as discussed in King *et al.*, 2004, [KIN1]). A simple example is the suggestion that most individuals in a given census area earn $50,000 p.a. based on the census return figure for the area in question, whereas there may be no individuals at all in this area matching this description — for example 50% might earn $25,000 p.a. and 50% $75,000 p.a., or many such combinations — from the aggregated data alone is is simply not possible to know. The problem of statistical grouping of data, described in the previous section (Statistics and Statistical Analysis, unemployment statistics example) illustrates some of the difficulties encountered when data is aggregated
- **Atomistic fallacy** — this fallacy involves ascribing characteristics to members of a group based on a potentially unrepresentative sample of members. As such it can be regarded as a central issue in statistical research, often related to sampling that is far too small or unrepresentative to enable such conclusions to be reached
- **Misinterpretation of visualizations** — there is endless scope for misinterpretation and there are many books on what makes for good and bad visualizations. The work of Edward Tufte (1983, [TUF1]) is amongst the best at providing guidance on what makes for good visualization. The emphasis should always be on clarity of communication, often achieved through simplicity in design and labeling. However, the apparently simple and clear chart can easily provide scope for confused reporting. For example, the data for the chart below was cited in the Summer 2007 issue of the USA *City Journal* in an article authored by David Gratzer M.D., in which he stated that says the U.S. prostate cancer survival rate is 81.2 percent and the U.K. survival rate is 44.3 percent. This apparently authoritative commentary was then picked up and used by leading US politicians. There are several problems with this interpretation of the graph. First, the data are from 7 years beforehand. Second, reported incidence simply reflects diagnosis rates, which in turn is related to the level of screening for the condition, which at the time was much more common in the USA than the UK. And finally, it is incorrect to deduce survival rates from the raw data on diagnosis and mortality rates. Survival rates require data that tracks the date of diagnosis to the lifespan of the individual. In broad terms the five-year relative survival rate for men

diagnosed in England in 2000-2001 was 71%. More details on survival rates for Prostate cancer over 1, 5 and 10 years can be found at the Cancer Research UK website

Prostate cancer incidence and mortality per 100,000 males per year



source: Anderson and Hussey (2000, [AND1])

Deliberate falsification of data

There are occasions when data is deliberately falsified. This maybe as a result of a rogue individual scientist or group, commercial enterprise and even government agency. The case of Prof Hwang Woo Suk who published fraudulent results on human cloning from stem cells in 2006 is one of the most famous (see https://en.wikipedia.org/wiki/Hwang_Woo-suk), but there is little doubt that deliberate or semi-deliberate falsification of data is more common than many realize. Deliberate omission of results that show no significant results or results that do not support a particular hypothesis can be regarded as a form of deliberate falsification and is a well-established problem in academic and medical research. Recent high-profile "fake news" cases highlight how modern media and lack of independent scrutiny can result in such issues becoming widely circulated.

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NASA Ozone watch information: http://ozonewatch.gsfc.nasa.gov

NADAQ 100-Index reference data: http://dynamic.nasdaq.com/dynamic/nasdaq100_activity.stm

2.3 Sampling and sample size

Sampling is central to the discipline of statistics. Typically samples are made in order to obtain a picture of the population as a whole without the need to make observations on every member of that population. This saves time, cost and may be the only feasible approach, perhaps because the population is infinite or very large or is dynamic so sampling provides a snapshot at a particular moment. Ideally we wish to make a sample that provides an extremely good representation of the population under study, whilst at the same time involving as few observations as possible. These two objectives are clearly related, since a perfect representation is only possible if the entire population is measured or if the population is completely uniform. This latter point highlights the fact that larger and more carefully structured samples may be required to obtain an estimate of a given quality if the population is highly variable. The difference between the measured value for an attribute in a sample from the 'true value' in the population is termed *sampling error*.

Typically a set of *n* independent samples are taken based on some form of random selection from the target population, as far as it is possible to define the latter. Randomness in the selection process seeks to help eliminate bias, whilst independence of samples also helps to ensure that bias due to samples being associated with each other in some way is minimized. For example, a sample of leaves from banana trees would seek to take one sample from each of a large number of banana trees that were relatively well separated spatially. It would be inappropriate to take 10 different samples from one tree (the samples would not be independent as they all came from the same tree) and likewise, trees in close proximity may exhibit similarities due to localized effects (e.g. soil, cultivation practice, disease spread etc.) which may result in samples not being independent. Similar considerations apply to samples taken from animals or humans, or from soils and rocks, and in some instances, samples take over a period of time where time dependencies exist. In cases where space- and/or time-dependencies are thought to exist, tests for autocorrelation should be carried out and if necessary, sample design and modeling must explicitly take account of the lack of independence between observations. The procedure adopted for any particular sampling exercise is known as the sampling protocol, and should always be carefully planned and designed.

Target Population

The first step in this process is to define the population of interest, from which samples are to be taken. The population may be finite or infinite, and may be very clearly defined (even if difficult to enumerate) — for example, "all adults over the age of 18 living in a given city", or may be less well defined — for example "particulates in the air over London", or "all measurements of outcomes from a particular industrial process". Ensuring the nature of the population to be studied is well understood is an important step in the initial design of any sampling scheme.

Study population

The study population is the collection of units that could possibly be measured (known as the *sampling frame* in survey work). In some instances samples are made on a population that can conveniently be studied (for example, sampling in a laboratory or a particular location) rather than sampling the population itself, with the results being applied to the real population of interest. This results in so-called *study error*, which again one seeks to minimize. In the example cited in The Statistical Method section, Michelson measured the speed of light in air on the Earth's surface, not the speed of light in a vacuum, so the study error in this case consisted of the difference between

these two environments. In many studies the research is carried out at a particular time and location, and the possible effects of temporal and spatial variation are excluded or deemed to have no substantive bearing on the results. However, all research does take place in space and time, so there is always some study error related to these factors. For example, after Michelson had completed his research, one criticism of it was that it was carried out during a brief period of the year, which did not allow for the possibility that the findings would have been different had the research been conducted 3 or 6 months later (reflecting the different position of the Earth relative to the Sun). It is often helpful to ensure that the study population is as tightly defined as possible, thereby ensuring that sampling is only from those individuals or objects that are of direct interest and helping to restrict variation in measured attributes.

Sampling protocol

This is the detailed procedure followed for sampling the data from the study population. In many instances the sampling protocol makes use of some level of randomization in order to avoid the risk of bias. The time, location and possible selection from subgroups of the study population form key elements of the sampling protocol. Controlled experiments typically involve use of a formal design that seeks to separate explanatory variables into distinct groups, which are then systematically or randomly sampled. In many instances random numbers are required in order to select entities, locations or times to be sampled, and typically these are computer-generated from a uniform distribution over the range [0,1]. Random numbers may also be drawn from other distributions, either using built-in software functions (e.g. the Excel Data Analysis tools Random Number generator facility, or SPSS functions of the form RV.DIST which returns a random value from a distribution DIST with specified parameters), or by using Uniform random numbers in conjunction with the cumulative distribution of interest.

In many instances a sample is required from an empirical distribution or a known (theoretical) distribution with pre-defined parameters. Typically this involves taking a random sample from the distribution selected or from a subset (e.g. a range) within this distribution. Many software packages provide facilities for generating such random samples, which may then be used to compare with observed datasets or as a frame for sampling (see further, Sampling from a known distribution).

When a large number of records have been obtained and stored in a database, samples from the dataset may be extracted for analysis rather than analyzing the full dataset (which might consist of thousands or millions of records). Typically samples of a pre-specified size are selected at random from the stored recordset, with checks made to ensure that key parameters do not vary too greatly from the population values (i.e. the sample is representative, not biased). Samples may be taken with or without replacement (without replacement is the norm) and may be stratified if necessary, depending on the manner in which the data is stored and grouped. Most statistical software packages provide a range of procedures for record selection. These vary from systematic to simple random, stratified random where selection probabilities are proportional to stratum size (PPS) and many variants on these. The table below lists the options provided for SPSS — other packages provide similar facilities. The documentation for SPSS, SAS/STAT and other packages provide exact details of how the variants (e.g. PPS Brewer vs PPS Murthy) are calculated. It is important to note that most standard statistical formulas assume that records are drawn from an infinite population by simple random sampling without replacement (WOR). If this is not the case the analytical tools applied must be adjusted to take the data selection procedure adopted into account. Again, statistical software that facilitates such non-random selection will also include facilities for computing core statistical measures and simple models adjusted for the sampling approach adopted.

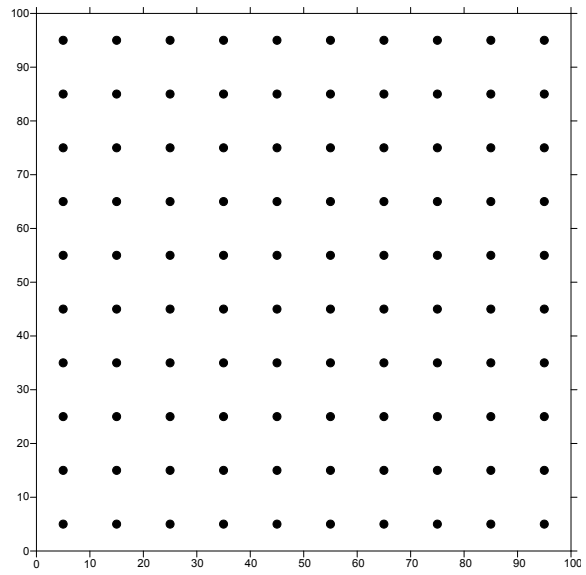
Sampling procedures — record selection sampling in SPSS

Simple Random Sampling	Units are selected with equal probability. They can be selected with or without replacement
Simple Systematic	Units are selected at a fixed interval throughout the sampling frame (or strata, if they have been specified) and extracted without replacement. A randomly selected unit within the first interval is chosen as the starting point
Simple Sequential	Units are selected sequentially with equal probability and without replacement
PPS	This is a first-stage method that selects units at random with *probability proportional to size* (PPS). Any units can be selected with replacement; only clusters can be sampled without replacement
PPS Systematic	This is a first-stage method that systematically selects units with probability proportional to size. They are selected without replacement
PPS Sequential	This is a first-stage method that sequentially selects units with probability proportional to cluster size and without replacement
PPS Brewer	This is a first-stage method that selects two clusters from each stratum with probability proportional to cluster size and without replacement. A cluster variable must be specified to use this method
PPS Murthy	This is a first-stage method that selects two clusters from each stratum with probability proportional to cluster size and without replacement. A cluster variable must be specified to use this method
PPS Sampford	This is a first-stage method that selects more than two clusters from each stratum with probability proportional to cluster size and without replacement. It is an extension of Brewer's method. A cluster variable must be specified to use this method
Use WR estimation for analysis	By default, an estimation method is specified in the plan file that is consistent with the selected sampling method. This allows you to use with-replacement (WR) estimation even if the sampling method implies WOR estimation. This option is available only in stage 1

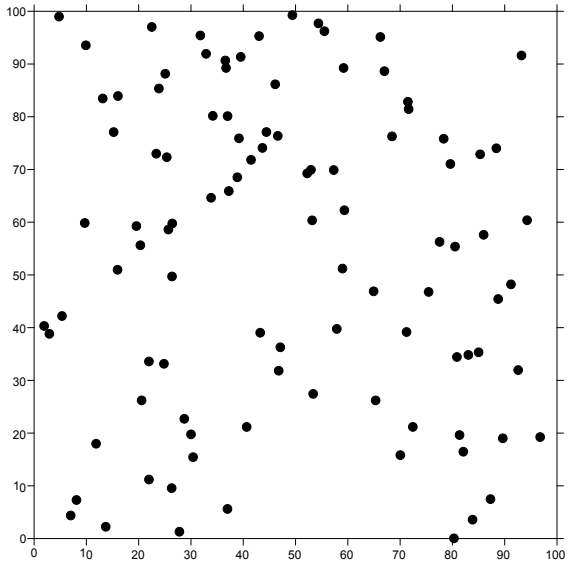
The above concepts apply, in somewhat modified form, to problems in higher dimensions. In particular, in two dimensions (spatial data selection) a number of special procedures may be required to ensure that samples are both randomly selected and yet are also representative (see further, de Smith *et al.*, 2018, section 5.1.2 [DES1]). As a simple illustration of the kind of approaches that can be adopted, the diagram below shows four methods for point sampling within a 100x100 unit study region. One interesting and important feature of this example is that approach B, which is simple random sampling, results in apparent spatial clustering of samples, whilst substantial areas are left unsampled. Sampling approach C is one means of trying to limit this affect. For more details see the reference cited.

Point-based sampling schemes

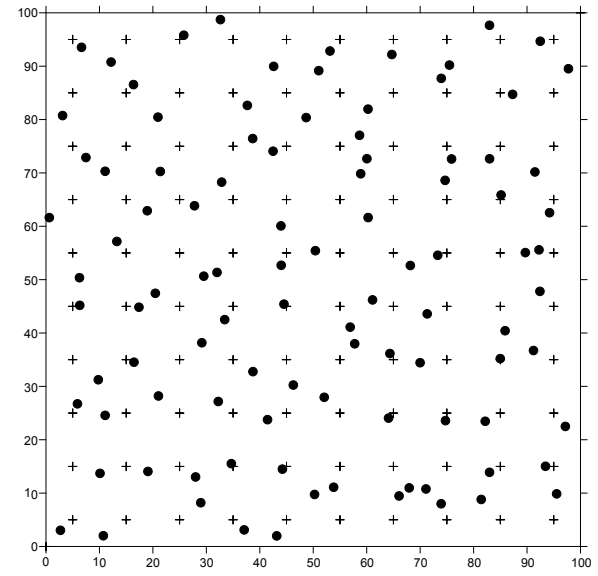
A. Regular



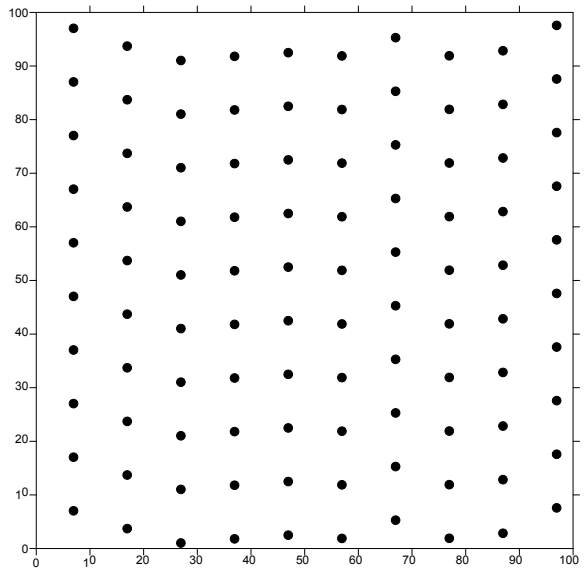
B. Random



C. Random offset from regular (random clustered)



D. Regular with random start of sequence (y offset)



Sample size

There are many factors that affect the choice of sample size. In public opinion surveys it is very common to hear that the sample taken was of around 1000-1500 people. This figure is obtained from a relatively simplistic calculation, based on achieving an approximately 95% confidence level in the results with estimation of a proportion, *p*, within a range of roughly +/-3% (see also, our discussion on confidence intervals). The figure of 1000-1500 arises from these two requirements — using a Binomial distribution the standard error (SE) of the proportion, *p*, is $\sqrt{(pq/n)}$. Note that the term $\sqrt{(pq)}$ is maximized for any given *n* when *p*=*q*=0.5, so this assumption provides an upper bound of 1/2 on $\sqrt{(pq)}$ and thereby on the range of expected variation in our estimate. Now from the Normal distribution, which is the limit of the Binomial for large *n* (and a reasonably rapid approximation if *p* and *q* are similar in size), we know that 95% of the distribution is included within roughly +/- 2 standard deviations. Thus the sample size needed to ensure an error in an estimate of x=5% is obtained from the formula for 2SEs, i.e. $1/\sqrt{n}$. This gives the result $n=1/x^2$ so for *x*=5%, x=0.05 we have *n*=400, or for 3% we have just over 1100. For a 1% range at 95%+ confidence a sample size of 10,000 would be required, so the choice of 1000-1500 is a compromise between the quality of estimation and the cost and time involved in undertaking the survey.

For some problems wider bands are acceptable on the estimated proportion or mean, thus for a value within +/-20% a sample of only 25 is required — if this was an estimate of the concentration of zinc in the soil in parts per million (ppm), an estimate of 100ppm with a range of 80-120ppm may be perfectly acceptable. This method of computing sample size is, of course, simply a rule of thumb that has been found to work in many situations of this particular type. Put more formally, we are estimating the probability, α, that the estimated proportion will not differ from the population proportion, *p*, by more than some amount *x*:

$$\Pr\left(|\, p-\hat{p}\,| \geq x\right) = \alpha$$

If we denote by z_α the Normal distribution probability value for a confidence interval determined by α (e.g. with α=0.025, two-tailed test, 5% in total, z_α=1.96) then this (rather simplified) formula for sample size *n* becomes:

$$n = z_\alpha^2 pq \big/ x^2$$

Sample size selection is thus related to several factors, including: (i) cost, time and risk; (ii) the type of problem being addressed (and the techniques used to address the problem); and (iii) the variability of the data being sampled. If one has prior knowledge of the data variability, or can make an informed estimate of this (for example based on prior research and/or test samples), then the determination of sample size becomes more straightforward. Clearly greater variability in the data will mean that the standard error (SE) is intrinsically larger, which in turn requires a bigger sample size for a given level of precision in the parameter(s) to be estimated. Furthermore, if the population is known to vary in some kind of structured (or *stratified*) manner, for example spatially or temporally, then it makes sense to sample less frequently in the less variable phases or zones and more frequently in those strata of the study population that are more variable. Thus a given overall sample size, *n*, might represent the sum of a set of stratified samples $\{n_i\}$, where each n_i is separately determined from the estimated variance, s_i, in zone or time slot *i*. There is an optimal method of determining the component samples given *n*, assuming that estimates of the variance in each zone, s_i, are available together with some measure of the proportions, w_i, of the overall population represented by each of the separate zones or strata. With countable items (e.g. census data) these proportions can be obtained as the count in zone *i* divided by the total for all

zones; other approaches might be to use areas or length of sampled time slots to determine the proportions. The basic allocation rule is then:

$$n_i = n\left(w_i s_i\right) \Big/ \sum_{i=1}^{k}\left(w_i s_i\right) \text{ , where } \sum_{i=1}^{k} w_i = 1$$

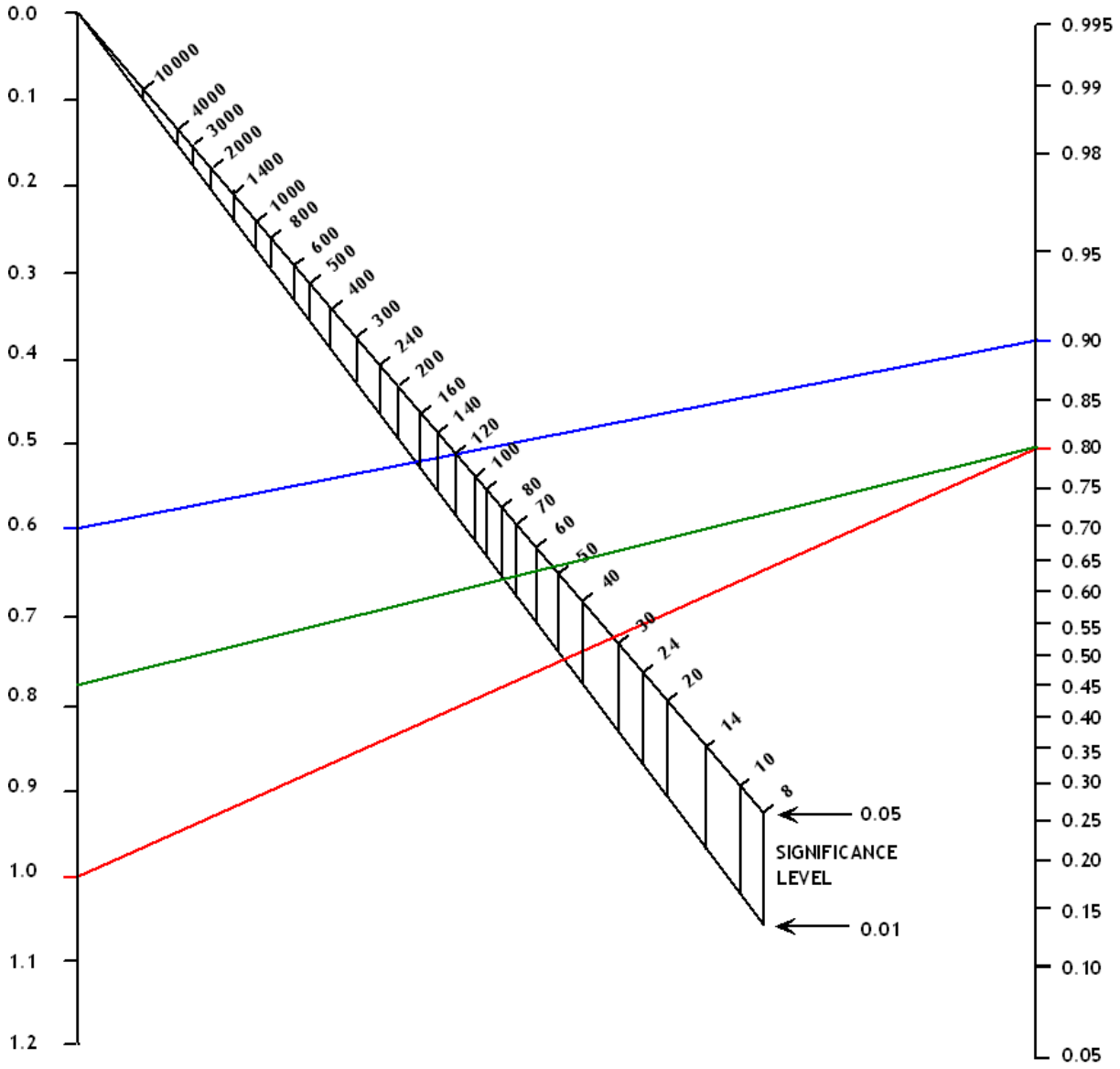
Note that this allocation simply determines how a given sample size (perhaps obtained with reference to some cost or time constraint) may be allocated amongst the selected strata.

Bartlett *et al*. (2001, [BAR1]) provide a general discussion of sample size determination for educational and social research, drawing on the earlier work of Cochran (1977, [COC1]). Their guidance draws on the experience of many researchers conducting questionnaire surveys and similar social research programmes. The formulas described are based on those discussed above, but take into account issues such as: finite population size; determination of the estimated variance; dealing with multiple measured variables of various types; and finally, dealing with non-response. Cochran recommends, for example, that if the sample size, *n*, exceeds 5% of the population size, *P*, then the sample size value should be adjusted by a factor $n/(1+n/P)$. Assuming an initial sample size estimate of 400 and a population of 4000, this would adjust the sample size down to 364. If the expected response rate is 60% the sample size is then increased to approximately 600.

A number of statistical tests, such as z-tests and t-tests, yield results that are dependent on the sample size, through the standard error. The sections that describe these tests also provide guidance on how to compute the sample size in order to meet requirements on the levels of Type I and Type II errors that are acceptable. Special graphs, known as Operating Characteristic curves, provide plots of the relationship between sample size and the two main types of error (see Ferris *et. al.*, 1946, [FER1], for a number of such charts covering χ^2, F, Normal or z-tests and t-tests).

In the medical field a range of sample size guidance documents, tables, software tools and formulas are available, many of which are effectively variants on the same general model (see Altman [ALT1], Chow, Shao and Wang [CHO1], Jones *et al* [JON1], Carley *et al.*[CAR1], Dupont and Plummer [DUP1], Whitley and Ball [WHI1], and Machin *et al.*[MAC1]). Typically sample size estimation in these publications is based on the relationship between three elements, two involving risk assessments and one involving the size of the effect one is seeking to discover (small effects require larger samples in order to detect them reliably): (a) the risk of a false positive (α level, usually taken as 5% or 0.05); (b) the risk of a false negative (β level, usually taken as 20% or 0.20; or using the notion of power=1-β, so 80%); and (c) the size of the effect. The last item can be difficult to determine, but is typically of the form: *E*=(target difference)/(estimated standard deviation). For example, if a study is trying to detect a difference of size 14 units between a measurement on two equal sized groups (e.g. the blood pressure in mmHg treated using different therapies, with measurements taken 6 hours after therapy commenced) and the estimated standard deviation was 18mmHg, then the standardized effect value would be 14/18=0.78. The chart below, redrawn from Altman [ALT1], enables the required sample size to be read from the central section by drawing a straight line between locations on the left and right hand axes. The left hand axis shows a measure of the size of effect one is trying to detect (in standardized units) whilst the axis on the right shows the power of the test (as noted above power=1-the risk of a Type II error or false negative). The third element, the risk of a Type I error or false positive is determined by the significance level in the central section.

Altman's Nomogram for computing sample size or power (two equal sized groups)



So if an experiment is to be defined that seeks to be able to identify a standardized effect of size 1.0 with a power of 80% and a risk of a Type I error of 5% we draw the red line (lowest on the nomogram)and choose an overall sample size of around 32, i.e. a target of 16 participants in each of two groups. If the power is increased (e.g. to 90%) and/or the effect size reduced (e.g. to 0.6) the required sample size increases to around 60 per group (120 total — blue line, upper line). For the blood pressure example cited earlier, a total sample size of 52 is required, as shown by the green (middle) line (26x2, based on an 80% power level). Note that this analysis can also identify trials that are inadequately powered, for example a trial that seeks to identify a relatively small effect with a sample size that is too small will equate to one whose power is low. Essentially these results are based on

the use of the (non-central) t-distribution in a t-test for the difference of two means where the population standard deviation is not known (see further, NIST and Beyer, Table IV.4 [BEY1] — note that these sources cite the sample size required for a single group).

Some have argued that this model is over-cautious and results in recommended sample sizes that are larger than are clinically necessary (with important ethical and practical implications), focusing instead on estimation based on clinical effect (e.g. benefits, harm). A related, alternative approach to sample-size determination, is to explicitly include measures of cost, in particular attempting to place a cost on each Type of error. The total cost is then the risk of a Type I error times the cost of this error plus the risk of a Type II error times the cost of this error plus the cost of the experiment or research exercise. This approach makes a great deal of sense, but allocating costs to the different types of error can be very difficult. If it is possible to produce such costs the impact of increasing sample size can be examined. In broad terms as sample size increases the Type I and Type II errors reduce so the costs associated with these risks will decrease, but the cost of the experiment will increase and may be infeasible for practical or ethical reasons. Incrementally increasing the sample size may achieve a result whereby total costs are minimized and this value can then be used for the research exercise.

Rare events

Particular issues arises in connection with rare events, for example when conducting trials of a vaccine that protects against a relatively rare disease, or when investigating suspected links between particular cancers and point sources of environmental pollution. In the former case, it may be necessary to carry out a trial involving very large numbers of individuals in order to identify a statistically significant effect. This was the case with early trials of the Salk Polio vaccine in the USA, in 1954, following Polio epidemics in 1952 and 1953. The estimated normal rate of infection at the time was around 50 per 100,000 population, but this still represented a large number of people (typically children). To obtain a target of approximately 100 confirmed cases of polio based on the normal incidence this would require a study group of 200,000 children. In the event, a randomized control trial (RCT) involving two groups of approximately 200,000 children using a double-blind assignment of subjects was undertaken — one group being given the Salk vaccine and the other a saline placebo. An extract of the core results are shown below — the success of the RCT led to the rapid roll-out of the Salk vaccine and then other, preferred vaccines, in the immediate aftermath, ultimately leading to the virtual eradication of Polio worldwide today. However, many aspects of the overall trial process were deeply flawed, with a large part of the trial (which was not in RCT form) described by Brownlee (1955, [BRO1]) as "futile" and "worthless".

USA Salk Vaccine Randomized Control Trial, 1954, Table 2b extract

Experiment	Study Group	Population	Polio Cases	
			Paralytic	Non-Paralytic
Randomized Control	Vaccinated	200,745	33	24
	Placebo	201,229	115	27

source: Francis and Korns (1955, [FRA1],[FRA2])

A simple form of analysis of this kind of data is to compute the effectiveness of the treatment by comparing the rates of infection per 100,000 in the vaccinated (r_1) and placebo (r_2) groups. The effectiveness measure is then E=100(1-r_1/r_2)% giving a result of E=72% in this case. Data of this kind can be analyzed in a number of different

ways. A simple approach is to consider the probability of observing x=33 or fewer paralytic cases of polio amongst those who were vaccinated as against 115 in the placebo group, both groups having been drawn from large equal sized populations. Using the null hypothesis that from a total of n=148 severe cases one would expect each group to have roughly half the total, hence p_0=0.5, we can use a simple z-transform of Binomial form:

$$z = \frac{x - np_0 + 1/2}{\sqrt{np_0(1-p_0)}} = \frac{33 - 74 + 1/2}{\sqrt{74/2}} = -6.7 \ (p < 0.001)$$

which is a very large value, hence extremely unlikely to have arisen by chance. By comparison, the number of non-paralytic cases were quite similar and very likely to have arisen by chance. This is the approach adopted by Francis and Korns [FRA2, Administrative content section, pp62-63].

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2.4 Data preparation and cleaning

Careful data preparation is an essential part of statistical analysis. This step assumes the data have been collected, coded and recorded, and now reside in some form of data store. This will often be in the form of a simple table (sometimes referred to as a *data matrix*) or SQL-compatible database. Depending on how the data were coded and stored, variables may or may not have suitable descriptions, coding or data types assigned, and if not, this is one of the first tasks to carry out. At this stage it will become apparent if any data items are incompatible with the data type assignments, for example text coded in numeric fields, or missing data that requires entry of a suitable 'missing data' code. Data provided from third parties, whether governmental or commercial, should include a metadata document that describes all aspects of the data in a standardized and thorough manner [UNI1].

Analysis of the dataset for duplicates is often the next step to undertake. There may be many reasons for duplicates existing in datasets, these include: genuine duplicates on one or more variables; data entry errors; multiple returns for the same case; duplicates on a subset of variables (as opposed to entirely duplicate records); and duplicates representing deliberate coding to the same reference. Depending on the nature and validity of the duplicates, decisions have to made on how they are to be treated. In some instances data will need to be de-duplicated, in others data will be retained unchanged, whilst in some instances additional data will be added to records to ensure the duplicates are separately identifiable. When analyzing duplicates using Exploratory Data Analysis (EDA) tools, duplicates may be hidden — for example, point maps of crime incidents frequently under-represent the concentration of crimes in certain locations as these are often recorded as co-located. Identification of duplicates may, of itself, be a form of EDA, identifying genuine co-incident results, or perhaps highlighting data coding protocols (such as assigning particular disease incidence to doctors surgeries or hospitals rather than the home address of the individual).

Zero and null (missing data) occurrences form a special group of duplicates that apply to one or more variables being studied. In many datasets the number of zeros recorded may be very large and their inclusion may totally distort analysis of the variables in question. Software tools may provide the option to mask out (i.e. hide) zeros from subsequent analysis. For example, a data collection device might record a value of an environmental variable, such as wind speed and direction, every 10 minutes. For perhaps 50% of all data items logged the speed might be below the threshold for measurement with the result that directional information also has no real meaning. Analysis of the dataset might choose to exclude the zero values from some EDA visualizations and statistical analyses, as these would overwhelm the results — this is not to say that such data be ignored, but that it should be separated for some parts of the analysis.

EDA methods will also tend to highlight exceptional data values, anomalies and outliers (specific measurements or entire cases) that require separate examination and/or removal from subsequent analysis. Note that this analysis is taking place on the source data, not post-processed information, although the measurement and recording process itself may have effectively pre-determined some of the possible characteristics of the source data (e.g. the coding applied, the resolution of measurement and recording equipment, any systematic data filtering applied during measurement or recording etc.).

In the case of outliers, there are several options of how they should be dealt with, and these will depend on the particular problem and form of analysis being considered. If the outlier is known to be an error (e.g. a mis-coding, by placing a decimal point in the wrong place) it can be corrected or removed. It may be an event of great interest, in which case it warrants separate examination and analysis — this again may result in the item(s) being

removed from the rest of the dataset. It can also be altered in a systematic manner, for example: changing the value to be 3 standard deviations from the mean; "Winsorizing" the value, whereby it is amended up or down to the adjacent value in a sorted series; or effectively excluded by computing statistics based on forms of trimmed measures, such as the trimmed mean.

Once a dataset has undergone preliminary inspection and cleaning, further amendments may be made in order to support subsequent analyses and the use of specific statistical models. It may be desirable for such amendments to result in the creation of a new data table or data layer, thereby ensuring that the source data remains untouched and available for re-inspection and analysis. In some instances (very large datasets) it is preferable to extract a representative sample of records and then apply modifications to this extracted set. Data in this new or modified layer may be subject to re-coding, grouping into new groups or classes, and/or apply some for of data transformation (for example applying a transformation to a continuous variable to improve the fit to the Normal distribution). A very large number of transformations are possible, many of these being supported in standard statistical analysis packages. For certain data types (such as temporal and spatial datasets) a specialized set of transformations are used, which reflect the serial and neighborhood aspects of such data. For example, with temporal data, various forms of temporal averaging, seasonal adjustments and filtering may be applied, whilst in spatial analysis such changes may be based on local, focal or zonal computations (see further, de Smith *et al.*, 2018, [DES1]).

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2.5 Missing data and data errors

Missing data is a wide-ranging term for the absence of expected data from a recorded sample, which may occur for many reasons and in many ways. In can be a small, easily managed problem, or a larger problem that raises questions about the usability of the dataset. Missing data can involve all relevant data for a record or set of records, or it could be missing values from a set of measurements relating to individual records (incomplete records). Each different situation requires separate consideration, both as to the seriousness of the problem, and to the means by which such difficulties are to be addressed. In the following paragraphs we discuss some examples of the key issues and approaches to resolving them. We then look in more detail at some of the techniques and tools provided within statistical software packages that are designed to assist in these situations.

In sample surveys the most common reasons are non-response, partial responses (only some questions answered) and spoiled responses. Surveys may be structured to ensure sample sizes are increased to a level at which the target response is achieved taking into account non-response and unusable responses, although this can be difficult when the survey involves quotas (e.g. the study must include responses from 50 women between the ages of 40 and 60, 50 between 60 and 80, and so forth). In general it is very difficult to avoid the problem that sample surveys or trials will yield incomplete response data, particularly where there are many questions or variables being examined. Such problems can lead to biased results and need to be addressed as early as possible in the overall data collection design and implementation phase of a project. Missing data may also be encountered when an experiment or trial is undertaken and unforeseen circumstances make some of the data unusable or impossible to obtain. For example, the present author conducted a controlled trial of three different types of multi-lingual keyboard in the European Commission headquarters in Brussels. A total of 96 staff were recruited (48 for week 1, 48 for week 2) to undertake computer-controlled typing tests in a variety of real and synthetic languages. All test sessions were completed with no data losses until one morning the building was picketed and attacked by French farmers protesting against proposed changes to the Common Agricultural Policy. They entered the building and were only removed after tear gas was used, which in turn shut down the lower levels of the building and our morning's data session was lost! Fortunately the exercise included enough replicates, including a complete replicate of the entire experiment in week 2, so analysis of the results was only marginally affected (see Evans, 1988 [EVA1]). In trials of medical procedures one or more of those involved in the trial may be unable to complete the trial due to illness or other, unrelated factors, or maybe one sample becomes contaminated or is not of the correct strength, so the data has to be discarded. This may be all the data relating to one or more participants in the trial, but more commonly relates to one or data items relating to a case — for example, a missing test result. Datasets that rely on remote-sensing equipment frequently demonstrate missing data, when equipment fails or has to be taken out of use temporarily for servicing or other reasons.

For certain experiments and analyses, such as some randomized block designs, loss of even a single data item is important because it upsets the balanced nature of the design and its subsequent analysis. Where observations are unavailable for a single unit this may be partially overcome by estimating or *imputing* the missing data from the remaining information, thereby turning the unbalanced design back to a balanced form. For example, in a randomized block design (see further, Cox, 1958 [COX1]) with k blocks and t treatments a simple estimate for a single missing value is given by $(kB-tT-G)/(k-1)(t-1)$ where B is the total of all remaining observations in the block containing the missing observation, T is the total of observations on the missing treatment, and G is the grand total. This provides a simple form of averaging for a single missing value — least squares techniques or simple iterative estimation can be used to extend the concept to more than one missing value. Analysis then continues as if the estimated value or values were genuine, but with residual degrees of freedom reduced by 1 for each missing

value and a correction for bias applied to the total sums of squares in the Analysis of Variance computation. Likewise, in time series analysis, complete time series are almost always required, making analysis of incomplete temporal datasets very problematic. Where such data is missing at the start or end of a series, it may be sufficient to simply ignore this problem and analyze the data that is available, assuming that it can be regarded as representative of the entire period. However, if embedded values (i.e. within the series) are missing some form of estimation is often the only option.

Another common reason for missing data is incorrect data recording, coding or subsequent processing. The precise reason for such errors and the scale of the problem are important to determine. Incorrect data coding by researchers and data preparation staff can often be checked through systematic verification, for example by taking a sample of each block of survey returns and having these independently recoded and compared with the original coding. Incorrect interpretation of survey questions, or incorrect recording of data by surveyed individuals, needs to be identified through inspection and validation techniques, thereby identifying the scale and nature of any problems, and implementing changes or corrections to the data gathering and/or subsequent processing of the data. The widely publicized issue of data quality associated with the Climate Science Unit (CSU) at East Anglia University in the UK (see http://www.cru.uea.ac.uk/cru/data/availability/ and the IPCC dataset site: http://www.ipcc-data.org/) provides a vivid insight into some of the issues associated with collating and cleaning datasets from multiple sources on a range of variables over a prolonged period of time.

Minor errors and occasional items of missing data can often be handled programmatically, but in some cases such approaches are not sufficient and the data and project will have to be reviewed in the light of the data limitations. Many software packages include facilities to handle problems with data completeness. The most common arrangement is for data to be coded to identify missing values, for example using a distinct entry such as a blank " ", * or -999 to indicate a missing value, depending on the data type and range being recorded. When an entry of this kind is encountered, the software package will apply one or more rules in order to determine what action to take. For example, in computing basic statistics for quantitative datasets it may simply ignore missing values (as opposed to deleting records with missing values) and carry out the computation on the available subset, with a reduced count of items. This raises the question as to whether such estimates are biased.

It is not merely the scale of missing items that must be considered, but also whether there is any pattern to the missing data. If the missing values occur completely at random (MCAR) and the proportion of missing values is not large (<5%) then statistics such as mean values, variances, correlations etc. can be produced ignoring these missing values and the results will tend to be unbiased. However, if the missing values are not randomly distributed throughout the data, bias will be apparent. It is possible that the non-randomness of missing values is partial, in the sense that within groups the missing values occur randomly but between groups there are substantial differences. This might be observed in cases where one group in more likely to respond to a question or to perform a task than another group. If the data show missing at random (MAR) data within groups but do not conform to the MCAR requirement, it is still possible to produced unbiased statistics within these groups. It may also be possible/acceptable to fill in missing values with estimated values that are derived from the remaining data in the entire study or subsets of the study — this applies principally to quantitative data in univariate and multivariate data sets, and to temporal and spatial datasets.

In order to determine whether MCAR, MAR or neither apply, the dataset can be partitioned and subject to various forms of simple pattern analysis and statistical comparisons. For example, all records could be divided into those with and without a data value on a given variable, and a comparison statistic (such as Little's chi-squared test, [LIT1, LIT2]) computed to try and detect any significant differences between the two subsets. Having identified

the scale and nature of the missing data problem, the question then arises as to what action to take. If the sample size is large enough and the proportion of records with missing data is small, it may be acceptable to either ignore the missing values (especially if the MCAR or MAR tests indicate that this is very safe to do), or to delete/ignore entire records with missing values (generally an unsafe practice, as this tends to introduce additional bias), or to impute the missing data (see further, below) from the remaining records. In this latter case missing data are essentially 'invented' by reference to other data in the sample. Typically results are then reported with and without the imputed data, with a clear explanation of the impact of imputation on the results.

There are many techniques for such imputation, notably maximum likelihood and a variety of regression methods. Pure multiple regression methods tend to underestimate the true variance of the imputed data values, so some form of variance inflation may be added to overcome this limitation. So-called multiple imputation (MI) methods are now favored by some researchers since these appear to provide more representative and robust results (see further, Pickles, 2005, [PIC1]). MI methods involve some form a conditional simulation, producing several imputations (typically 5-10) and then using the mean of the results as the estimates for the missing values. Alternatively the entire analytical procedure can be carried out on each of the versions of the dataset, and the results from each analysis averaged or compared. Typically such methods will compute the mean and variance of the variable across records for which complete data is available and then sample random values from the Normal distribution matching these parameters to obtain sample values for the missing item. Some packages, such as SAS/STAT, perform MI using samples obtained via MCMC methods (essentially this involves using the remaining data as a model distribution for the missing data and randomly sampling from this model distribution). For categorical data samples are taken from a Multinomial distribution. Another approach, which is sometimes usable with categorical data, is to create a new category that contains those records that include missing data.

Similar concepts have been applied in temporal and spatial analysis, both as a form of missing data analysis and as a form of prediction or estimation for unsampled times and locations. For example, the use of conditional simulation is now a preferred form of prediction in geospatial engineering applications, such as oil and mineral prospecting. If there are very few missing data points in dense temporal or spatial datasets it is usual for these to be estimated using deterministic procedures, using linear, bi-linear or spline interpolation from their immediate or near-neighboring data items, or using simple mean or median values in the local neighborhood. The quality of imputed results can be evaluated by comparison with the entire dataset (e.g. convergence of parameters), by internal consistency checks (e.g. jackknifing and bootstrapping techniques) and/or by reference to external datasets and samples (e.g. so-called 'ground truth' comparisons).

Handling missing values — techniques and tools

This section provides a brief summary of the main approaches for handling missing values. In most instances these are procedures offered within software packages, but it remains the responsibility of the researcher to select the method used and to document and justify such selection when reporting the results of analysis. In many cases estimating missing values will apply to real-valued measurements, but some procedures may apply to binary or categorical data.

Ignoring entire records

This is the most commonly available approach for handling missing data. As noted above, this is only acceptable if the number records is relatively large, the number of records with missing data is relatively small (<5%), and the missing records can be shown to occur completely at random (MCAR) or are missing at random (MAR) within well-

defined subsets of the data. In general this approach cannot be used in small sample balanced trials nor for time series.

Setting missing values to fixed value

Many packages allow missing values to be replaced with a fixed value (e.g. 0) or a user-provided value for each instance. The problems of adopting these approaches are obvious.

Single estimation procedures

A very common approach to missing values is to use some form of estimation based on the characteristics of the data that has been successfully collected. For example, the SPSS Transform operation, Missing Values option, offers the following options for estimating such values: (i) use of the mean or median value of nearby points (by which it means neighboring records, with the number of such records used selectable by the researcher); (ii) use of the overall series mean, i.e. the mean based on all records; (iii) linear interpolation, which applies to data in series and uses the two adjacent non-missing values, to fill in the gap or gaps; (iv) linear regression, which is similar to linear interpolation but use a larger number of neighboring points and calculates a best fit line through these as its estimator for intermediate missing values. Other software packages may provide additional options — for example, a variety of model-based interpolation options are available in the SAS/ETS (Economic and Time Series) software. Similar procedures are provided in some other packages, but often it remains the researcher's responsibility to provide or compute estimates for missing values as a part of the data cleaning and preparation stage.

Multiple imputation (MI)

Multiple imputation (MI) methods vary depending on the type of data that is missing and the software tools used to estimate (impute) the missing values. In this subsection we describe the approaches adopted by the SAS/STAT and SPSS software, which are largely based on the published work of Rubin (1976, 1987, 1996 [RUB1],[RUB2], [RUB3]).

Essentially there are 3 stages to MI:

- the missing data are filled in *m* times to create *m* complete datasets (*m* is typically 5)
- the *m* complete datasets are analyzed separately, in the usual manner
- the results from the multiple analyses are combined in order to provide statistical inferences regarding the data

Depending on the type and pattern of missing data, SAS/STAT and SPSS will generate estimates for the missing values using some form of regression analysis of the valid data (single, multiple or logistic regression), or MCMC methods under an assumption of multivariate Normality, for more general missing values. The latter approach is of the general form: (a) initialize estimates for the missing values for all records and variables by drawing random values from a Normal distribution with mean and variance that match the non-missing data (or use a multinomial distribution for categorical data, with proportions in each class defined by the proportions in the non-missing data); (b) using all the data, except for missing data on the j^{th} variable, use a univariate method (e.g. regression) to impute the missing values in that variable; (c) iterate across all variables and track the convergence of both the mean and variance of the imputed missing values.

When the datasets are analyzed the results are combined to produce a single set of inferences together with the between and within imputed dataset covariances. As Rubin (1996, p476, [RUB3]) explains, the posterior

distribution of the data obtained following multiple imputations is simply the average of the individual imputations, the mean values are the means of the imputations, and the variances are the sum of the average of the individual variances obtained from the MI process plus the variance of the mean values obtained.

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2.6 Statistical error

When approaching any form of data analysis many types and sources of error may be considered: the data collection procedure may contain errors; there may be gross data capture or encoding errors; there may be errors in the approach adopted to selecting data, designs or in analysis. However, none of these relates to the rather special use of the term *statistical error*. This term refers specifically to *non-systematic or random errors* that are observed during measurement. There may be many reasons why such random variations occur, but in general the assumption is made that these reasons are unknowable and therefore cannot be readily removed. Systematic variations and gross errors can, at least in theory, be separated out and either accounted for or removed, leaving simply statistical error.

2.7 Statistics in Medical Research

Statistical methods as applied to problems in medical research are, at first sight, no different from the application of such methods to any area of scientific endeavor. However, there are some important societal and technical aspects of medical research that warrant particular attention. At the societal level the issues relate to the impact on individual patients of intervention procedures, treatments and their side effects. The conduct and interpretation of medical trials is an extremely important issue, and decisions made regarding who is to be treated and how, and who is not to be treated, are often complex and can be distressing for all involved. Furthermore, inadequate design, implementation and reporting of trials can lead to erroneous conclusions, with potentially serious consequences. On a technical level there are specific techniques and protocols that have been developed to address many of these issues, but there remains continuing difficulties facing medical staff who need to understand and use appropriate statistical procedures whilst having an enormous number of other issues to deal with. Again, these problems can be addressed by early involvement of medical statisticians, although the scarcity of experienced specialists in this field is an additional concern. There is also an ongoing debate regarding the appropriateness of classical frequentist statistics, and even Bayesian statistics to many problems in medical research, bearing in mind the practical complexities and uncertainties associated with such work, especially for observational studies.

In 1937, the editor of The Lancet, writing in the foreword of Austin Bradford Hill's groundbreaking book "Principles of Medical Statistics" [BH1] summarized the position of statistics in medicine at that time as follows:

> *"In clinical medicine today there is a growing demand for adequate proof of the efficacy of this or that form of treatment. Often proof can come only by means of a collection of records of clinical trials devised on such a scale and in such a form that statistically reliable conclusions can be drawn from them. However great might be our aversion to figures, we cannot escape the conclusion that the solution of most of the problems of clinical or preventative medicine must ultimately depend on them"*

Bradford Hill sought to provide an easily understood introduction to statistical concepts and methods for medical students, and his book [BH1] continued to be updated and published in many editions and in many translations, over a period of forty years. He was particularly concerned to ensure that the foundations of medical research benefited from sound underlying logical analysis and testing. To this end he was one of the initial proponents of randomized controlled trials (RCTs), which provide a key framework for current medical research exercises. In addition he devised a series of *viewpoints* on how suspected cause-effect relationships can be evaluated. Both of these areas are discussed in more detail below.

Bradford Hill was also extremely influential in bringing the idea of cohort studies to the fore through his work with Sir Richard Doll on the link between smoking and lung cancer. Their initial research was based on a case-control approach, but they then extended this work to a cohort study of over 30,000 British doctors. Cohort studies typically involve tracking the medical histories of a select group or *cohort* of individuals over many years. For example, in 2010 an international cohort study known as COSMOS was launched. The UK cohort will follow the health of approximately 100,000 mobile phone users (18+ years old) for 20-30 years, and the international cohort will follow approximately 250,000 European mobile phone users over this period.

Considerable efforts have been made by many specialists with the aim of improving the understanding of statistics by medical professionals and in ensuring the quality of reporting in journal publications is of the highest standard (see especially the excellent article and associated discussion in Altman and Bland, 1991 [ALT1]). The quality of published studies has been greatly aided by the production or adoption of guidelines by individual journals, and by

the development of "statements" that explain how different types of research exercise should be reported. Perhaps the most important of these is CONSORT: "Consolidated Standards of Reporting Trials", which encompasses various initiatives to alleviate the problems arising from inadequate reporting of randomized controlled trials (RCTs). We discuss CONSORT further below. Other examples of such statements include STROBE "Strengthening the Reporting of Observational studies in Epidemiology", and the EQUATOR network, which is an international effort that seeks to "improve the reliability and value of medical research literature by promoting transparent and accurate reporting of research studies". Their 'reporting guidelines' section includes links to many useful websites and articles, including those already mentioned, and articles such as Olson *et al*. [OLS1] on the reporting of case-control studies.

As mentioned earlier, undertaking and reporting of medical research requires many specialized skills. Historically there has been insufficient training of medical researchers in statistical concepts and methods, and very real problems of communication between medical and statistical specialists. For example, the terms *significance*, *variance* and *frequency* may have a very different meaning to medical staff from those assigned by statisticians. To medics *significance* has the more usual interpretation of 'being significant' or *important* in the context of the medical problem under consideration — indeed, statisticians and medical journals now often play down the use of the term and the associated use of statistical significance levels (*p*-values). Estimation (identifying the typical range of values/effects) is rightly regarded as being of far greater relevance. For those involved in case-mix management (CMM) *analysis of variance* may refer to financial management (variation from targets) rather than having any statistical interpretation, whilst *frequency* can refer to how often a patient visits the toilet! As with many disciplines, technical terminology unfortunately may serve to confuse rather than clarify the subject.

There is no simple answer to these problems, although modern undergraduate and post-graduate teaching practice attempts to address the most important issues in a manner that medical specialists are most likely to respond to and retain, long after the brief courses given have been completed. The leading medical journals, key medical reference web sites, the early involvement of medical statisticians, statistical consultancy and peer review, recently published precedents and the application of sound methodologies (such as the PPDAC model discussed earlier in this Handbook) will all serve to assist those engaging in medical research and trials for the first time.

The technical statistical procedures applicable to medical research are covered in the various main topics and sections of this Handbook. However, there are one or two specific topics that warrant further comment at this juncture. The two we have focused upon are Causation, and the Conduct and Reporting of Research. Each of these topics is discussed briefly in the subsections that follow.

An equally important topic, which is of particular relevance to medical research, is that of Bayesian analysis. We have discussed aspects of Bayesian analysis earlier in this Handbook (e.g. see Yudowsky's example of breast cancer screening). Whilst not excluding classical frequentist statistics, a substantial number of scientists believe that Bayesian thinking is essential in the medical sphere — as Professor Campbell states in his commentary on Altman and Bland's paper (see also [CAM1]):

> *"Many doctors have an 'a priori' belief that the patient either has or does not have the disease and use the Bayesian paradigm to modify their beliefs. They find the idea of a null hypothesis existing without any probability attached to it counter-intuitive"*

Other authors argue that for some problems only a Bayesian approach can provide a sensible answer, or in some instances, any answer at all.

We now take a closer look at the thorny question of causality, and how suspected cause-effect relationships can be identified and studied. We then consider some aspects of the conduct and reporting of medical research, including randomized controlled trials (RCTs), case-control studies and cohort studies. These procedures are a particular feature of modern medical research and RCT in particular is a development that has been largely championed in the medical statistics field.

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2.7.1 Causation

In our earlier discussion of the problems associated with using and interpreting statistical data we described some of the difficulties involved when trying to establish and model causation. As Rothman *et al.* (2008, p5 [ROT1]) observe:

> *"such a model should address problems of multifactorial causation, confounding, interdependence of effects, direct and indirect effects, levels of causation, and systems or webs of causation"*

In medical statistics the word *cause* is often used in a probabilistic sense, i.e. by suggesting that factor A is a cause of outcome or disease B, we often mean that A significantly increases the risk or probability of outcome B. This lack of specificity reflects an underlying uncertainty about the detailed processes at work. Hence recognizing that a particular chemical is carcinogenic does not explain the processes that lead from exposure to incidence of the condition — these processes are likely to be extremely complicated involving molecular biology, and may be difficult if not impossible to determine.

In a famous paper delivered by Austin Bradford Hill to the Royal Society of Medicine in 1965 [BH2], he suggested a series of *viewpoints* (his terminology) by which one might use as guidance when seeking to establish the nature and validity of a suspected causal relation. In this subsection we summarize what has now become known as the *Bradford Hill Criteria*, although the term *criteria* was not used in his paper. He commences with the assumption that a clear-cut association (or correlation) of some kind has been observed. This association is not assumed to be one that has been obtained as statistically significant — in fact, Bradford Hill argues strongly against the blind use of statistical significance in this context. In addition and as noted above, the causal relationship may in fact be complex, as for example in a causal chain, or in an effect that may be the result of multiple (i.e. different) causal factors or the result of several factors working in combination. Bradford Hill's nine viewpoints for examining possible causal effects are, in summary:

Bradford Hill's (1965) 9 Viewpoints for Causation

1. Strength: if an association is very strong it deserves closer consideration than weaker associations — for example, if we observe that heavy smokers are 30+ times more likely to contract lung cancer than non-smokers, the strength of evidence is more powerful than if we observed that they were only 2x as likely to contract lung cancer. In fact it was Bradford Hill who first brought this particular relationship to public attention. On the other hand, lower strength of evidence does not imply that there is no causal relationship
2. Consistency: is the observed association repeated/repeatable, in different locations, at different times and under differing circumstances? As above, the absence of such repeatability does not imply that there is no causal relationship — for example, it may not be possible to repeat a set of circumstances
3. Specificity: if the observed association appears to be highly specific to a given set of circumstances and/or locations, then it is more likely to be related to these circumstances in some causal manner. For example, the very high incidence of certain diseases amongst individuals working in very specific environments (e.g. chimney sweeps in the 18th and 19th centuries; Nickel refinery workers in the early 20th century). A somewhat different example is the incidence of pre-menopausal breast cancers where a high number of cases has been observed within particular families across the generations, suggesting a specific genetic effect
4. Temporality: here the question is whether the order is $A \rightarrow B$ or $B \leftarrow A$. For example, is being extremely overweight causing people to contract a particular disease or condition, or do people with a particular condition become extremely overweight. These kinds of relationships can be quite subtle and inter-connected
5. Biological gradient: if increased exposure to some well-defined hazard is associated with a similarly increase in disease incidence, then this tends to support a causal relationship, as compared with a relationship for which no 'gradient effect' is observed
6. Plausibility: if the suspected causal relationship is plausible, within the scope of current knowledge, then it has (marginally) more merit than a relationship for which no known explanation can be proposed. Having made this observation, it is clearly a relatively weak criterion
7. Coherence: if the suspected causal relationship is consistent with current knowledge about the variables involved, it may help to support (or at least, not to detract from) the possible causal relationship being considered. Again, as with plausibility, this may be regarded as a relatively weak criterion
8. Experiment: if one or more repeatable controlled experiments can be carried out to test the suspected causality, and these tests support the hypothesis, this greatly enhances the strength of evidence case
9. Analogy: if a similar causal relationship has been established, but under different circumstances, it may again provide support for the argument that a causal relationship exists, but again this is a weak criterion

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These 9 viewpoints have been taught to students in the biomedical sciences for many years, often as criteria rather than as broad guidance. More recently authors such as Phillips and Goodman [PH1] have re-emphasized the original 'lessons' of Bradford Hill, in particular his skepticism regarding the use of statistical significance. In their commentary they summarize these missing lessons as:

- Statistical significance should not be mistaken for evidence of a substantial association
- Association does not prove causation (other evidence must be considered)
- Precision should not be mistaken for validity (non-random errors may exist)

- Evidence (or belief) that there is a causal relationship is not sufficient to suggest action should be taken
- Uncertainty about whether there is a causal relationship (or even an association) is not sufficient to suggest action should not be taken

In preparing these bullet points the authors were particularly concerned to address the question of systematic errors or bias, which we have previously seen can be complex and inadvertently introduced, thereby confusing both intuitive and statistical inference. They also emphasize the importance of the relationship between causal analysis and the subsequent decision making regarding policies such as screening, interventions and vaccination. The latter exists in a much broader framework of political and economic considerations, requiring weighted cost-benefit and risk-based assessments, whatever the apparent strength of evidence may be from causal analysis.

Evans (1976, (EVA1]) focused on identification of cause-effect relationships for diseases, rather than the generality of such relations. His "*criteria* for causation" table, developed as a form of unification of the ideas and research by many authors over the previous century, but curiously without reference to Bradford Hill, is provided below (with *his italics*):

Evans' (1976, Table 13) 10 Criteria for Causation

1. Prevalence of the disease should be significantly higher in those exposed to the putative cause than in cases [or] controls not so exposed
2. Exposure should be present more commonly in those with the disease than in controls without the disease when all the risk factors are held constant
3. Incidence of the disease should be significantly higher in those exposed than in those not exposed as shown in prospective studies
4. Temporally, the disease should follow exposure with a distribution of incubation periods on a bell shaped curve
5. A spectrum of host responses should follow exposure along a logical biological gradient from mild to severe
6. A measurable host response following exposure should regularly appear in those lacking this before exposure or should increase in magnitude if present before exposure
7. Experimental reproduction of the disease should occur in higher incidence in animals or man appropriately exposed than in those not so exposed; this exposure may be deliberate in volunteers, experimentally induced in the laboratory, or demonstrated in a controlled regulation of natural exposure
8. Elimination or modification of the putative cause or the vector carrying it should decrease the incidence of the disease
9. Prevention or modification of the host's response on exposure should decrease or eliminate the disease (e.g. immunization, application of statins to reduce cholesterol), and
10. Sense: the whole thing should make biologic and epidemiological sense

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There are a number of formal and informal tools and procedures that may be utilized to assist in the analysis of the relationships between supposed causes and effects (i.e. in addition to purely statistical approaches). In many fields, including medical research, structured diagrams are often helpful, for example the use of traditional graph theory such as the work of Greenland *et al.* [GR1, ROT1] which uses the analysis of directed acyclic graphs (DAGs)

to help identify and understand cause-effect relationships and confounding. A number of authors in the medical field have also used the Ishikawa or *fishbone* diagram as an aid to identifying the components and structure of causation particularly in the context of quality management and policy making. Formal structured review procedures, such as brainstorming and Delphi techniques, and of course the entire peer review process for research work and publications, collectively provide a range of mechanisms for obtaining the best possible understanding of possible cause-effect relationships.

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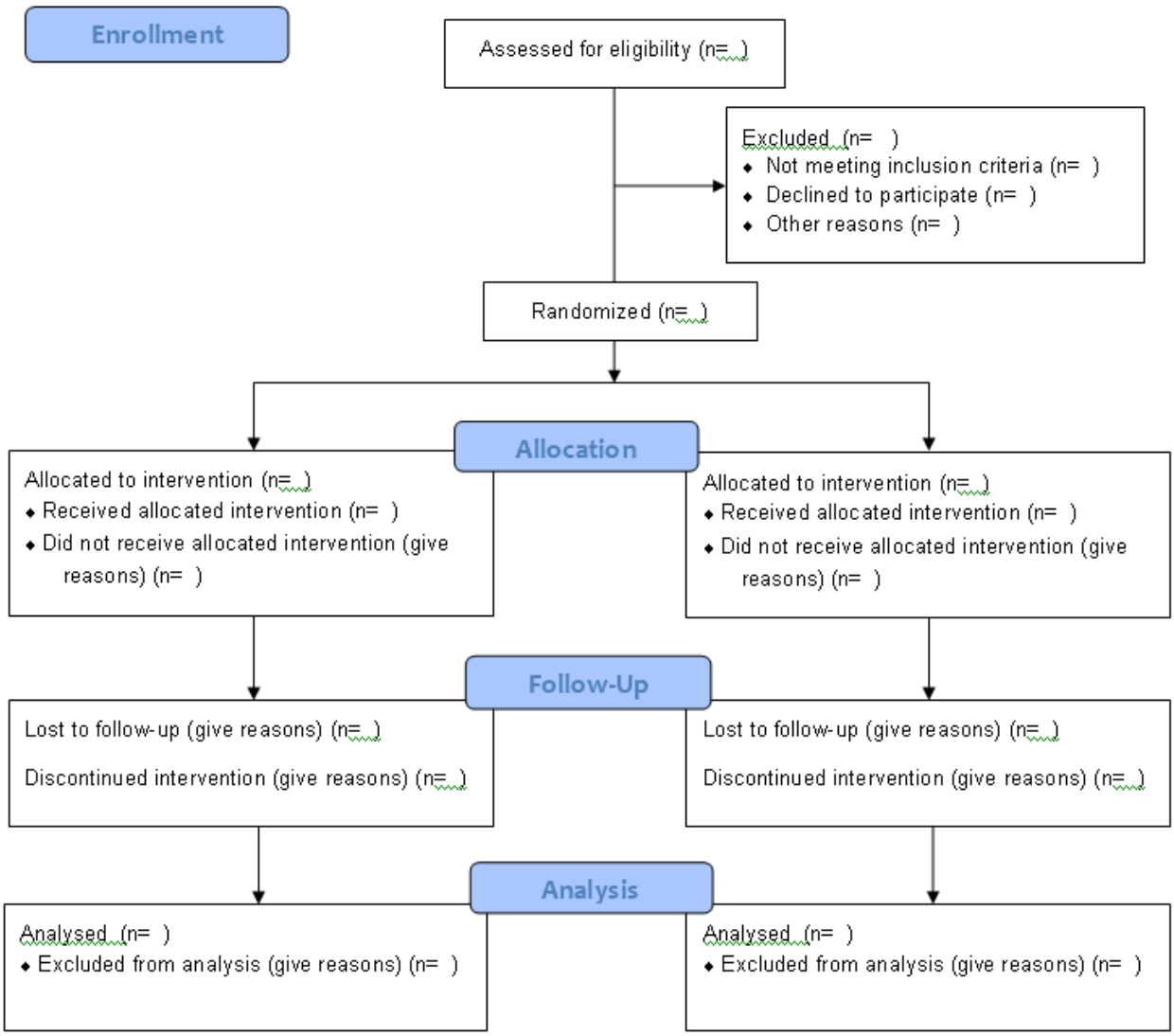
2.7.2 Conduct and reporting of medical research

When planning any substantive piece of medical research, especially where human patients are involved, great care in the design of the research is required. Whilst the PPDAC methodological framework described above has broad applicability to such problems, there are specific considerations that make such exercises in the medical arena particularly problematic (e.g. see the discussion in Ercan *et al.*, 2007 [ERC1]). Many of these are addressed through adoption, where practicable, of a procedure known as randomized controlled trials, or RCTs. In its simplest, and most widely used form, the RCT is a relatively straightforward procedure — at least, in theory! Other widely used forms of medical research include case-control studies and cohort studies. All three of these procedures are described in greater detail in the subsections that follow.

Assuming a trial or other form of study has been designed and is undertaken, the question of reporting all steps in the process is paramount. In recent years there has been a great deal of effort put into standardizing the registration of the details of trials (essentially metadata), and into structured reporting. This has been led by the academic community in association with all the major medical journals, and has led to a series of "statements" that are designed to both assist and direct the conduct of trials. Journals such as Annals of Internal Medicine, BMC Medicine, BMJ, Journal of Clinical Epidemiology, the Lancet, Obstetrics & Gynecology, Open Medicine, PLoS Medicine and Trials have all adopted and published guidelines for reporting randomized trials under the CONSORT

or "Consolidated Standards of Reporting Trials" initiative. CONSORT 2010 is the latest version of these guidelines, and comprises specifically the process of reporting what was done and what was found (i.e. it does not include recommendations for designing, conducting or analyzing trials). Essentially CONSORT consists of a checklist for publication which covers: Title and abstract; Introduction; Methods; Randomization; Results; Discussion and Other information. It also includes a flow diagram "of the progress through the phases of a parallel randomized trial of two groups", which we have included below. More details can be found on the CONSORT website and in the references below. There are also a number of extensions to the CONSORT statement that provide guidance for different forms of trials, such as cluster trials (e.g. where treatments are applied to clusters, such as members of a family) and a number of other forms of trial.

CONSORT 2010 FLOW DIAGRAM



As noted above, RCT's are by no means the only, or always the best or most appropriate framework for the conduct of medical trials. In many instances the 'ideal' of a controlled experiment is not achievable, and many other forms of research are also widely used — for example cohort studies and case-control studies. However, the great advantage of RCT's is that they have been shown, within the strict confines of the trial in question, to be the best means for avoiding bias and minimizing confounding effects, enabling conclusions regarding the differences between outcomes to be made with a relatively high degree of confidence.

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STROBE (Strengthening the Reporting of Observational studies in Epidemiology): http://www.strobe-statement.org/

CONSORT (Consolidated Standards of Reporting Trials) encompasses various initiatives to alleviate the problems arising from inadequate reporting of randomized controlled trials (RCTs): http://www.consort-statement.org

EQUATOR Network: http://www.equator-network.org/

Wikipedia: Randomized controlled trials: http://en.wikipedia.org/wiki/Randomized_controlled_trial

2.7.2.1 Randomized controlled trials

The randomized controlled trial (RCT) is generally accepted as the preferred approach to conducting a wide variety of medical trials and is a central technique in the broader field of evidence-based medicine. The advantages of the approach are many, but in particular they have been shown to be very effective in controlling for selection bias and confounding, which other procedures may fail to achieve. In order to explain the central ideas behind RCTs, we start by providing a brief description below of the steps involved in the very first RCT, which was designed to determine the effectiveness of a new treatment for tuberculosis (TB).

The first step when designing an RCT is to carefully define the problem to be studied. Ideally this definition should be easily understood and as narrow as is practical. In the British Medical Research Council's (MRC) study of tuberculosis treatments in the late 1940s, the trial (of the effectiveness of streptomycin as a treatment) was

defined by restricting it to: "*acute progressive bilateral pulmonary tuberculosis of presumably recent origin, bacteriologically proved, unsuitable for collapse therapy, age group 15 to 25 (later extended to 30)*" [BH1; Ch.20, and [MRC1]). This particular trial was the first truly randomized clinical trial and this aspect of the trial was devised by Austin Bradford Hill — he himself had been diagnosed with TB and spent two years in hospital and a further two years convalescing from the disease in his early 20s.

The second step, in the most commonly applied form of RCT, is to consider two distinct groups, ideally of approximately equal size and make-up. In the tuberculosis trial 55 patients were given the new treatment (Streptomycin plus bed rest) whilst a separate group of 52 patients were just given bed rest. One group is the *treatment group* (or intervention group) whilst the other is the *non-treatment group* or *control group*. By non-treatment we mean that this group receives a placebo, or no treatment, or continues on an existing, established treatment programme — the approach chosen must be precisely defined.

The patients selected to be involved in the trial are then randomly allocated to one of the two groups and their progress monitored over a period of time (usually relatively short). Most RCTs now carried out follow this general approach. There are other variants, notably cross-over RCTs, where patients are randomly assigned to groups but are then randomly re-assigned so they receive a sequence of treatments or non-treatments.

In the case of the 1948 tuberculosis trial the results after 6 months were as follows:

	Streptomycin	Control
Considerable improvement	28 (51%)	4 (8%)
Lesser improvement or deterioration	23 (42%)	34 (65%)
Deaths	4 (7%)	14 (27%)

This finding was regarded as being an important breakthrough, both in terms of the success of the treatment, which was both clear to see and statistically significant (i.e. is extremely unlikely to have occurred by chance). After 12 months a further 8 of the treated patients had died, and a further 10 of the control group, again a significant result, but also indicating a reduced efficacy of the treatment over time. None of the patients, however, could be regarded as having been cured. Interestingly enough, at the time the authors did not report why they chose the sample sizes used. In a remarkable recorded interview in 1990 Bradford Hill, then aged 93, stated that the main reason for choosing 50 or so patients was that this was as much Streptomycin as could be obtained from the USA at the time given its scarcity, high cost and the considerable problems in obtaining US currency in the UK in the immediate post-WWII period. He also stated that the patients were not informed about the treatment they were to receive. The authors also do not describe what form of statistical analysis was performed, merely that the results were statistically significant — the impression one has from Bradford Hill's book is that simple chi-square tests were carried out.

In order to carry out the random assignment of patients to groups, researchers originally used simple random selection by patient number, possibly stratified into blocks (e.g. by sex and by age grouping) but this can lead to problems. An example is given by Cancer Research UK:

"it is possible to be biased without realizing it. For example, if a new treatment has quite bad side effects, the doctors running the trial might subconsciously avoid putting sicker patients into the group having the new treatment. So as the trial went on, the control group would have more and more of the sickest patients in it. The people in the new treatment group would then do better than the control group. So, when the trial results come out, the new treatment would [incorrectly] look as if it works better than the standard treatment."

To avoid such problems a system known as blinding is applied. In *blind trials* one or more parties are unaware of the assignment of treatments. For example, in a so-called single-blind trial the individual receiving the treatment is not made aware whether the treatment they are being given is an existing treatment, a new treatment or a placebo (i.e. a tablet or preparation that is not a drug at all and has no effect on the patient). In double-blind trials neither the experimenter nor the patient know which treatment has been assigned to which patient (treatments are coded) thereby minimizing the risk of any influence the experimenter may have on the experiment. Unfortunately this terminology is not uniformly applied, leading to current recommendations to describe in detail the kind of blinding applied (if any), even extending to those involved in analysis and interpretation of the results.

Whilst the RCT procedure described above appears simple and straightforward, it does have numerous difficulties. Determining the appropriate sample size to use can be problematic, especially in the case of rarer conditions and/or where suitable triallists are simply not available in the location or at the period of time required (see the earlier discussion on sample size, and in particular, the Salk Polio vaccine trials of 1954). The cost of conducting such trials may be high, and if the trial is interrupted during its structured program, or there are problems with adverse effects or triallists dropping out, how are the results to be interpreted? Some treatments are not amenable to such form of trial, for example those requiring specific actions or exercises by participants. Sample size determination can be difficult and it may be impossible to obtain the desired numbers in each group and stratum or the required sample size if far larger than is achievable within time and cost constraints. There are also often ethical problems — for example, should a particular treatment that is thought to be very promising be withheld from very sick patients? (see further, the Declaration of Helsinki).

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Wikipedia: Randomized controlled trials: http://en.wikipedia.org/wiki/Randomized_controlled_trial

2.7.2.2 Case-control studies

Case-control studies involve investigations that are essentially retrospective in nature, since they involve the study of patients who have acquired a disease or condition, and comparing these cases with so-called 'controls' whose profile is similar to the cases. By similar we mean that the controls have not exhibited the condition under investigation but have considerable similarities with those who have — for example, they have the same age/sex mix, they live in the same area, do similar work, attended similar schools etc. In some instances case-control studies involve multiple control groups, but more typically there is one group of cases and another of controls. In other instances multiple diseases that affect cases, or different levels of severity of cases, are analyzed simultaneously, which obviously complicates the design. As with other forms of medical research procedures, we

provide an example below to illustrate the typical application of this approach. In this example we consider the analysis of data relating to the incidence of a particular disease amongst individuals who have been exposed to some infectious agent, substance or environmental factor which is suspected as being causative. The simplest model is to assume that the row and column totals are known and fixed and then to apply Fisher's exact test to the results. This model evaluates the hypothesis that the results show no association between disease incidence and exposure and is a simple and clear procedure.

Example: Esophageal cancer cases in Brittany

In the example table below we show the incidence of esophageal cancer amongst males in part of Brittany in France (200 cases) and a sample of 775 males (the controls) selected at random from the local electoral lists in the same region. Examining the tabulated summary results we see that the odds of being a high consumer of alcohol for cases is 96:109 (i.e. almost 1:1) whereas for controls the ratio is 104:666 (around 1:7). The odds ratio is thus (96/109)/(104/666)=5.64. Put another way, the data suggest that you are at least 5 times more likely to suffer from esophageal cancer if you are a heavy drinker than if you are a more moderate drinker. To place this into context, a 125ml glass of 8% strength wine (very weak, most wines are 12-13%) equates to 10gms of alcohol or one unit (in international measure), with the current recommended daily maximum consumption being 2 units for women (20mg) and 3 units (30mg) for men.

Alcohol consumption	80+g/day	<80g/day	Total
Cases	a=96	b=109	205
Controls	c=104	d=666	770
Total	200	775	n=975

This data and its analysis is discussed in detail in Breslow and Day (1980, [BRE1]). The lower case letters identify the notation used in many studies, with the odds ratio being computed simply as ad/bc.

We can compute Fisher's exact statistic for this 2x2 table, and the chi-square approximation, on the hypothesis that the entries are independent. The chi-square statistic yields a value of 110.26 (unadjusted) or 108.22 with Yates adjustment, both highly significant. The exact test, using Fisher's method as implemented in R, also confirms that the result is highly significant and also provides the odds ratio, as above, together with a 95% confidence interval for this ratio of [3.94,8.06]. These values are the so-called Cornfield confidence intervals (Cornfield, 1956, reported in Breslow and Day [BRE1]). These statistical tests can be seen as test of the hypothesis that the odds ratio equals 1 against the alternative that it is greater than 1.

The data under discussion have been greatly simplified — detailed information which is available has been summarized in a 2x2 table. Whilst this is helpful and demonstrates an apparently very strong relationship between the incidence of this type of cancer with high alcohol consumption, it disguises potentially important information and possible confounding factors. For example, it was known that the individuals in the control data in this study were, on average, 10 years younger than the case data. Since alcohol consumption may vary with age, perhaps an age-related confounding factor exists. Indeed, since the ages of cases and controls are known, the data could be stratified by age group and each stratum analyzed separately. The odds ratios for each group can be computed and compared to see how homogeneous these are, assuming sufficient data exists at each stratum level for such a comparison. Likewise, the division of alcohol consumption into two levels rather than more is somewhat arbitrary, thus analysis of cases and controls could be extended to obtain a more detailed picture of this relationship (with

or without age-based stratification). Clearly as the number of levels and strata are increased, so the cell entries will diminish and without relatively large samples the scope for detailed breakdowns of this type will be limited. Also, the Fisher test for tables with more than a 2x2 arrangement is typically implemented using simulation methods. Finally, the dataset also collected information on tobacco consumption — perhaps the strong relationship observed for alcohol consumption is actually not causative but indicative of lifestyle. By including tobacco consumption levels as well as alcohol consumption, for cases and controls, estimates of relative risks (by age group) can be obtained.

For the above analysis controls were not tightly matched to cases — for example, their age profile, and possible other important factors, were not matched. In some instances carefully matched controls can be identified which generally increases the power of the analysis. Typically more controls than cases are identified, and analysis proceeds either by taking the first or a randomly selected matched control from a set, or by combining the controls as if they represented a single individual. Procedures for analyzing matched controls, which are variants of those described above, are covered in Breslow and Day [BRE1]. For more complex problems it may be preferable to apply techniques based on logistic regression, with unmatched or matched samples.

References

[BRE1] Breslow N E, Day N E (1980) Statistical Methods in Cancer Research: Volume 1 — The Analysis of Case-Control studies. IARC Scientific Publications No.32, World Health Organization, IARC Lyon

[BRE2] Breslow N E, Day N E (1987) Statistical Methods in Cancer Research: Volume 2 — The Design and Analysis of Cohort Studies. IARC Scientific Publications No.82, World Health Organization, IARC Lyon

[MAN1] Mantel N, Haenszel W. (1959) Statistical aspects of the analysis of data from retrospective studies of disease. Journal of the National Cancer Institute, 22, 719-748

2.7.2.3 Cohort studies

Cohort studies primarily consist of the selection of a group of individuals (the cohort) and studying aspects of their development over many years, possibly several decades. In particular, disease incidence and mortality of the cohort are studied. As with case-control studies and randomized control trials, the unit of analysis is the individual, i.e. macro-level relationships amongst groups (i.e. population correlation or ecological studies) are not the basis for research in any of these methods. At the start of the process members of the cohort are recruited, generally with a carefully constructed profile that is designed to embrace the study population of interest, and detailed interviews are conducted to learn relevant information about their background, health history, lifestyle etc. Further interviews and/or questionnaires are then conducted every few years over the course of the project. The great advantage of this approach, which is known as a *prospective cohort study*, is that information about the individuals is well documented and all subsequent disease incidence is recorded, in many cases up to eventual death. However, this may take a long time and may exhibit only a few cases of the specific disease or diseases of interest unless a very large cohort is used, which increases the cost and complexity of the project. *Retrospective or historical cohort studies* seek to identify a group or cohort with known exposure to a suspected agent, and then attempt to reconstruct the history of exposure and related data in order to obtain an understanding about current disease incidence and mortality patterns. This approach has the advantage that data is available relatively quickly and without excessive expense, may be the only possible approach (for example if a substance or circumstance not longer applies), but is subject to many practical problems — notably missing data and recall problems.

Prospective cohort studies may be compared with a case-control approach, for which cases are selected from those with a disease of interest, controls are selected, and the two datasets are compared. For example, in the very first major cohort study, that of British Doctors commencing in 1951, some 34,440 male doctors were recruited to the study, and after 20 years total incidence of lung case deaths was 441. This compares with a case-control study that commenced in 1948 and was completed in 1952, with 4342 people being involved and 1488 being lung cancer cases. The advantages of case-control studies for identifying possible relationships of importance is clear, and they are much faster and typically less costly to conduct, but they are severely limited in the degree of confidence in the nature of the relationship and by their reliance on recalled information. With a cohort study an improved understanding of the relationship between exposure, lifestyle and outcomes is possible, including effects not previously identified. For example, in the British Doctors study it was apparent, after 20 years, that the death rate amongst heavy smokers from all causes was twice that of non-smokers. In this example the level of long-term successful follow-up of the cohort was very high, but in other studies this has not been the case. Unless the results are available for a very high proportion of the cohort, the validity of the results may be called into question.

In summary, Breslow and Day [BRE2] identify the following advantages of cohort studies as compared with case-control studies. Cohort studies:

- Give a wider picture of the health hazards associated with a given exposure
- Eliminate most forms of selection bias and recall bias
- Are often the only practical option where exposure to specific agents (e.g. suspected hazardous industrial chemicals) is rare
- In addition to detailed interviews or questionnaires, medical tests can be carried out at the start of the cohort study that may aid interpretation of outcomes, for example in terms of prior susceptibility to certain conditions
- Repeated measurements over the lifetime of the study may be possible and important — for example, measurements of specific chemicals present in blood or urine samples
- Absolute risk rates are obtained for the cohort, as opposed to relative risk rates for case-control studies. However, if the cohort is not representative of the broader population these risk estimates cannot be extended without reservation

Historically, most attention has been focused on mortality whereas more recently interest has been shown in a combination of severity of various conditions (e.g. chronic illnesses) and the detail of dose-response relationships, both of which are more demanding in terms of data (e.g. obtaining an understanding of multi-factor effects) and analytical methods. For dose-response analysis much emphasis is placed on fitting alternative models to data collected over time, using various forms of time series analysis to help model, and thereby predict safe exposure or dose levels in absolute and temporal terms.

References

[BRE1] Breslow N E, Day N E (1980) Statistical Methods in Cancer Research: Volume 1 — The Analysis of Case-Control studies. IARC Scientific Publications No.32, World Health Organization, IARC Lyon

[BRE2] Breslow N E, Day N E (1987) Statistical Methods in Cancer Research: Volume 2 — The Design and Analysis of Cohort Studies. IARC Scientific Publications No.82, World Health Organization, IARC Lyon