

Chapter 1 : Life table - Wikipedia

This is the first volume to present a comprehensive treatment of the theory and application of life table techniques. The emphasis is placed on applications, and the theory is presented in such a way that individuals with minimal knowledge of calculus and matrix algebra can follow the argument.

Direct methods[edit] Direct data comes from vital statistics registries that track all births and deaths as well as certain changes in legal status such as marriage, divorce, and migration registration of place of residence. In developed countries with good registration systems such as the United States and much of Europe , registry statistics are the best method for estimating the number of births and deaths. A census is the other common direct method of collecting demographic data. A census is usually conducted by a national government and attempts to enumerate every person in a country. In contrast to vital statistics data, which are typically collected continuously and summarized on an annual basis, censuses typically occur only every 10 years or so, and thus are not usually the best source of data on births and deaths. Analyses are conducted after a census to estimate how much over or undercounting took place. These compare the sex ratios from the census data to those estimated from natural values and mortality data. Censuses do more than just count people. They may also collect data on migration or place of birth or of previous residence , language, religion, nationality or ethnicity or race , and citizenship. Map of countries by population Rate of human population growth showing projections for later this century Indirect methods[edit] Indirect methods of collecting data are required in countries and periods where full data are not available, such as is the case in much of the developing world, and most of historical demography. One of these techniques in contemporary demography is the sister method, where survey researchers ask women how many of their sisters have died or had children and at what age. With these surveys, researchers can then indirectly estimate birth or death rates for the entire population. Other indirect methods in contemporary demography include asking people about siblings, parents, and children. Other indirect methods are necessary in historical demography. There are a variety of demographic methods for modelling population processes. The United Kingdom has a series of four national birth cohort studies, the first three spaced apart by 12 years: These have followed the lives of samples of people typically beginning with around 17, in each study for many years, and are still continuing. As the samples have been drawn in a nationally representative way, inferences can be drawn from these studies about the differences between four distinct generations of British people in terms of their health, education, attitudes, childbearing and employment patterns. The general fertility rate , the annual number of live births per 1,000 women of childbearing age often taken to be from 15 to 49 years old, but sometimes from 15 to The age-specific fertility rates, the annual number of live births per 1,000 women in particular age groups usually age , etc. The crude death rate , the annual number of deaths per 1,000 people. The infant mortality rate , the annual number of deaths of children less than 1 year old per 1,000 live births. The expectation of life or life expectancy , the number of years that an individual at a given age could expect to live at present mortality levels. The total fertility rate , the number of live births per woman completing her reproductive life, if her childbearing at each age reflected current age-specific fertility rates. The replacement level fertility, the average number of children women must have in order to replace the population for the next generation. For example, the replacement level fertility in the US is 2.1. The net reproduction ratio is the expected number of daughters, per newborn prospective mother, who may or may not survive to and through the ages of childbearing. A stable population, one that has had constant crude birth and death rates for such a long period of time that the percentage of people in every age class remains constant, or equivalently, the population pyramid has an unchanging structure. It can be expanding or shrinking. For example, the number of deaths per 1,000 people can be higher for developed nations than in less-developed countries, despite standards of health being better in developed countries. This is because developed countries have proportionally more older people, who are more likely to die in a given year, so that the overall mortality rate can be higher even if the mortality rate at any given age is lower. A more complete picture of mortality is given by a life table , which summarizes mortality separately at each age. A life table is necessary to give a good estimate of life expectancy. Basic equation[edit] Suppose that a country or other

entity contains Population persons at time t .

Chapter 2 : What are Stem Cells? Types of Stem Cell and their Uses

Chapter 4 is concerned with life tables based on survey and observational data, while Chapter 5 is devoted to comparisons of life tables. Chapters 6, 7, and 8 are devoted to multiple-decrement life tables, dealing as they do with 2 or more ways of exit from a given state.

Not all stem cells come from an early embryo. In fact, we have stem cells in our bodies all our lives. One way to think about stem cells is to divide them into three categories: You can read in detail about the properties of these different types of stem cells and current research work in our other fact sheets. Here, we give you a short overview of different stem cell types before comparing the progress made towards therapies for patients, and the challenges or limitations that still need to be addressed. Embryonic stem cells ESCs have unlimited potential to produce specialised cells of the body, which suggests enormous possibilities for disease research and for providing new therapies. ESCs are what is called pluripotent, that means they can differentiate into any cell type of the body. Human ESCs were first grown in the lab in The cells are derived from a developmental stage, when about cells form a so called blastocyst – a very early embryo. But not every experiment requires a new blastocyst. As of October , about different cell lines, each derived from a single embryo, were obtained in Europe source human pluripotent stem cell registry. These cell lines need to be very well characterised for scientists to use them in clinical trials or drug development – another reason which limits the number of embryonic stem cell lines. Current challenges facing ESC research include ethical considerations and the need to ensure that ESCs fully differentiate into the required specialised cells before transplantation into patients. It also allows the generation of iPSC cell banks, which would work almost like blood banks, where a matching donor can be found for patients. However, use of iPSCs in cell therapy is theoretical at the moment. The technology is very new and the reprogramming process is not yet well understood. Scientists need to find ways to produce iPSCs safely and more efficiently. The cells must also be shown to completely and consistently differentiate into the required types of specialised cells to meet standards suitable for use in patients. Many tissues in the human body are maintained and repaired throughout life by stem cells. These tissue stem cells are very different from embryonic stem cells. Tissue stem cells, are not pluripotent like ESCS, but multipotent. That means they can only make a limited number of specialised cell types that are specific for their organ of origin; neural stem cells, for example, can only differentiate into specialised brain cells, whereas blood stem cells can only form specialised cells of the blood system. Stem cells are important tools for disease research and offer great potential for use in the clinic. Some adult stem cell sources are currently used for therapy, although they have limitations. The first clinical trials using cells made from embryonic stem cells have just finished, but further studies are needed before any therapeutics for more patients can be approved. Meanwhile, induced pluripotent stem cells are already of great use in research, but a lot of work is needed before they can be considered for use in the clinic. All other clinical trials rather involve the derivation of iPSCs from patient cells either for disease modelling, drug testing or to increase our understanding of the basic biology of this cell type. An additional avenue of current research is transdifferentiation – converting one type of specialised cell directly into another. All these different research approaches are important if stem cell research is to achieve its potential for delivering therapies for many debilitating diseases.

Chapter 3 : Demography - Wikipedia

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Boston University School of Public Health Introduction This module introduces statistical techniques to analyze a "time to event outcome variable," which is a different type of outcome variable than those considered in the previous modules. A time to event variable reflects the time until a participant has an event of interest e. Statistical analysis of time to event variables requires different techniques than those described thus far for other types of outcomes because of the unique features of time to event variables. Statistical analysis of these variables is called time to event analysis or survival analysis even though the outcome is not always death. What we mean by "survival" in this context is remaining free of a particular outcome over time. The questions of interest in survival analysis are questions like: What is the probability that a participant survives 5 years? Are there differences in survival between groups e. Learning Objectives After completing this module, the student will be able to: Identify applications with time to event outcomes Construct a life table using the actuarial approach Construct a life table using the Kaplan-Meier approach Perform and interpret the log rank test Compute and interpret a hazard ratio Interpret coefficients in Cox proportional hazards regression analysis Time to Event Variables There are unique features of time to event variables. First, times to event are always positive and their distributions are often skewed. For example, in a study assessing time to relapse in high risk patients, the majority of events relapses may occur early in the follow up with very few occurring later. On the other hand, in a study of time to death in a community based sample, the majority of events deaths may occur later in the follow up. Standard statistical procedures that assume normality of distributions do not apply. Nonparametric procedures could be invoked except for the fact that there are additional issues. Specifically, complete data actual time to event data is not always available on each participant in a study. In many studies, participants are enrolled over a period of time months or years and the study ends on a specific calendar date. Thus, participants who enroll later are followed for a shorter period than participants who enroll early. Some participants may drop out of the study before the end of the follow-up period e. In each of these instances, we have incomplete follow-up information. True survival time sometimes called failure time is not known because the study ends or because a participant drops out of the study before experiencing the event. What we know is that the participants survival time is greater than their last observed follow-up time. These times are called censored times. Censoring There are several different types of censoring. The most common is called right censoring and occurs when a participant does not have the event of interest during the study and thus their last observed follow-up time is less than their time to event. This can occur when a participant drops out before the study ends or when a participant is event free at the end of the observation period. These issues are illustrated in the following examples. A small prospective study is run and follows ten participants for the development of myocardial infarction MI, or heart attack over a period of 10 years. Participants are recruited into the study over a period of two years and are followed for up to 10 years. The graphic below indicates when they enrolled and what subsequently happened to them during the observation period. During the study period, three participants suffer myocardial infarction MI, one dies, two drop out of the study for unknown reasons, and four complete the year follow-up without suffering MI. The figure below shows the same data, but shows survival time starting at a common time zero i. Based on this data, what is the likelihood that a participant will suffer an MI over 10 years? Their observed times are censored. In addition, one participant dies after 3 years of follow-up. Should these three individuals be included in the analysis, and if so, how? The fact that all participants are often not observed over the entire follow-up period makes survival data unique. In this small example, participant 4 is observed for 4 years and over that period does not have an MI. Participant 7 is observed for 2 years and over that period does not have an MI. While they do not suffer the event of interest, they contribute important information. Survival analysis techniques make use of this information in the estimate of the probability of event. An important assumption is made to make appropriate use of the censored data. Specifically, we assume that censoring is independent or

unrelated to the likelihood of developing the event of interest. This is called non-informative censoring and essentially assumes that the participants whose data are censored would have the same distribution of failure times or times to event if they were actually observed. Now consider the same study and the experiences of 10 different participants as depicted below. Notice here that, once again, three participants suffer MI, one dies, two drop out of the study, and four complete the year follow-up without suffering MI. However, the events MIs occur much earlier, and the drop outs and death occur later in the course of follow-up. Should these differences in participants experiences affect the estimate of the likelihood that a participant suffers an MI over 10 years? In survival analysis we analyze not only the numbers of participants who suffer the event of interest a dichotomous indicator of event status , but also the times at which the events occur. Introduction to Survival Data Survival analysis focuses on two important pieces of information: Whether or not a participant suffers the event of interest during the study period t . The follow up time for each individual being followed. Follow Up Time Time zero, or the time origin, is the time at which participants are considered at-risk for the outcome of interest. In many studies, time at risk is measured from the start of the study t . In a prospective cohort study evaluating time to incident stroke, investigators may recruit participants who are 55 years of age and older as the risk for stroke prior to that age is very low. In a prospective cohort study evaluating time to incident cardiovascular disease, investigators may recruit participants who are 35 years of age and older. In each of these studies, a minimum age might be specified as a criterion for inclusion in the study. Follow up time is measured from time zero the start of the study or from the point at which the participant is considered to be at risk until the event occurs, the study ends or the participant is lost, whichever comes first. In a clinical trial, the time origin is usually considered the time of randomization. Patients often enter or are recruited into cohort studies and clinical trials over a period of several calendar months or years. Thus, it is important to record the entry time so that the follow up time is accurately measured. Again, our interest lies in the time to event but for various reasons e . For participants who do not suffer the event of interest we measure follow up time which is less than time to event, and these follow up times are censored. The Survival Function In survival analysis, we use information on event status and follow up time to estimate a survival function. Consider a 20 year prospective study of patient survival following a myocardial infarction. In this study, the outcome is all-cause mortality and the survival function or survival curve might be as depicted in the figure below. Sample Survival Curve - Probability Of Surviving The horizontal axis represents time in years, and the vertical axis shows the probability of surviving or the proportion of people surviving. At time zero, the survival probability is 1. At 2 years, the probability of survival is approximately 0. At 10 years, the probability of survival is approximately 0. The median survival is approximately 11 years. A flat survival curve i . The figure above shows the survival function as a smooth curve. In most applications, the survival function is shown as a step function rather than a smooth curve see the next page. The figure below shows Kaplan-Meier curves for the cumulative risk of dementia among elderly persons who frequently played board games such as chess, checkers, backgammon, or cards at baseline as compared with subjects who rarely played such games. Adapted from Verghese et al. Estimating the Survival Function There are several different ways to estimate a survival function or a survival curve. There are a number of popular parametric methods that are used to model survival data, and they differ in terms of the assumptions that are made about the distribution of survival times in the population. Some popular distributions include the exponential, Weibull, Gompertz and log-normal distributions. Other distributions make different assumptions about the probability of an individual developing an event i . More details on parametric methods for survival analysis can be found in Hosmer and Lemeshow and Lee and Wang^{1,3}. We focus here on two nonparametric methods, which make no assumptions about how the probability that a person develops the event changes over time. Using nonparametric methods, we estimate and plot the survival distribution or the survival curve. Survival curves are often plotted as step functions, as shown in the figure below. Time is shown on the X-axis and survival proportion of people at risk is shown on the Y-axis. Note that the percentage of participants surviving does not always represent the percentage who are alive which assumes that the outcome of interest is death. The median survival is 9 years i . Consider a small prospective cohort study designed to study time to death. The study involves 20 participants who are 65 years of age and older; they are enrolled over a 5 year period and are followed for up to 24 years

until they die, the study ends, or they drop out of the study lost to follow-up. In the study, there are 6 deaths and 3 participants with complete follow-up i. The remaining 11 have fewer than 24 years of follow-up due to enrolling late or loss to follow-up.

Chapter 4 : Life-tables and their demographic applications | Health Knowledge

Get this from a library! Life table techniques and their applications. [N Krishnan Namboodiri; C M Suchindran] -- This is the first volume to present a comprehensive treatment of the theory and application of life table techniques.

Background[edit] There are two types of life tables: Period or static life tables show the current probability of death for people of different ages, in the current year Cohort life tables show the probability of death of people from a given cohort especially birth year over the course of their lifetime. Static life tables sample individuals assuming a stationary population with overlapping generations. If a population were to have a constant number of people each year, it would mean that the probabilities of death from the life table were completely accurate. Also, an exact number of , people were born each year with no immigration or emigration involved. Life tables can be constructed using projections of future mortality rates, but more often they are a snapshot of age-specific mortality rates in the recent past, and do not necessarily purport to be projections. For these reasons, the older ages represented in a life table may have a greater chance of not being representative of what lives at these ages may experience in future, as it is predicated on current advances in medicine, public health , and safety standards that did not exist in the early years of this cohort. A life table is created by mortality rates and census figures from a certain population, ideally under a closed demographic system. This means that immigration and emigration do not exist when analyzing a cohort. A closed demographic system assumes that migration flows are random and not significant, and that immigrants from other populations have the same risk of death as an individual from the new population. Another benefit from mortality tables is that they can be used to make predictions on demographics or different populations. One being that they do not state the overall health of the population. There is more than one disease present in the world, and a person can have more than one disease at different stages simultaneously, introducing the term comorbidity. Other characteristics can also be used to distinguish different risks, such as smoking status, occupation, and socioeconomic class. Life tables can be extended to include other information in addition to mortality, for instance health information to calculate health expectancy. Health expectancies such as disability-adjusted life year and Healthy Life Years are the remaining number of years a person can expect to live in a specific health state, such as free of disability. Two types of life tables are used to divide the life expectancy into life spent in various states: Multi-state life tables also known as increment-decrements life tables are based on transition rates in and out of the different states and to death Prevalence-based life tables also known as the Sullivan method are based on external information on the proportion in each state. Life tables can also be extended to show life expectancies in different labor force states or marital status states. Life tables that relate to maternal deaths and infant mortalities are important, as they help form family planning programs that work with particular populations. To do this, actuaries develop mathematical models of the rates and timing of the events. They do this by studying the incidence of these events in the recent past, and sometimes developing expectations of how these past events will change over time for example, whether the progressive reductions in mortality rates in the past will continue and deriving expected rates of such events in the future, usually based on the age or other relevant characteristics of the population. The availability of computers and the proliferation of data gathering about individuals has made possible calculations that are more voluminous and intensive than those used in the past i. This is particularly the case in non-life insurance e. However the expression "life table" normally refers to human survival rates and is not relevant to non-life insurance. Life table for the total population: United States, , Page 8 The basic algebra used in life tables is as follows.

Chapter 5 : Survival Analysis

This is the first volume to present a comprehensive treatment of the theory and application of life table techniques. The emphasis is placed on applications, and the theory is presented in such a way that individuals with minimal knowledge of calc.

We are currently in the process of updating this chapter and we appreciate your patience whilst this is being completed. One important method of assessing the health of a population is to ask how long people can expect to live. Life expectancy, usually reported at birth although it can be applied to other ages as well, is a commonly used summary measure which can also be used to compare against countries. Life expectancy is calculated using life tables. A life table is a table which shows, for a person at each age, what the probability is that they die before their next birthday. From this starting point, a number of statistics can be derived and thus also included in the table is: Life tables are usually constructed separately for men and for women because of their substantially different mortality rates. Life tables are also used in biology. Construction of life tables Age specific mortality rates are applied to a notional population, typically of , Starting at birth, the probability of dying in each period is applied to the number of people surviving to the beginning of the period, so that the initial figure slowly reduces to zero. The different elements required for a life table include using standard notations: In contrast, actual life expectancy of a particular birth cohort can only be calculated when everyone in this cohort is dead. This approach uses a cohort life table and requires data over many years to prepare just a single complete cohort life table. Example An example of how a life table can be constructed and the mathematics involved can be downloaded from the simple interactive statistical analysis website [http: Strength](http://Strength) Summary measure of mortality providing an overall picture of mortality, allowing countries and regions to be compared. It does not say much about who is still alive, and their quality of life; for example, how many years are lived with disability before dying. This has led to attempts to bring together morbidity and mortality, with measures such as Health Adjusted Life Expectancy and Disability Adjusted Life Years. Health Adjusted Life Expectancy HALE This is calculated by subtracting from the life expectancy a figure which is the number of years lived with disability multiplied by a weighting to represent the effect of the disability. This raises all sorts of moral questions on who defines and measures disability level and how they do it. Weightings were applied to conditions by using the time trade off approach, in which people were asked to consider living more years in imperfect health compared with fewer years in perfect health. The study also placed more weight on the life of a young adult compared with a new born. PYLL can be expressed absolutely or as a rate relative to the population at risk. Other applications Other characteristics can also be used to distinguish different risk factors for life expectancy, such as smoking-status, occupation, socio-economic class, and others. More complex analyses for assessing cancer survival, that involves comparisons between two populations or a population in two points in time can also be undertaken. In addition to public health domains, life tables are also used by insurance companies and actuary departments. When used in biology, age specific fertility rates are also included in the calculations. When data have not been available, such as in low income countries, life tables have been modelled using what data are available, usually childhood mortality data.

Of all published articles, the following were the most read within the past 12 months.

Box , Riyadh , Kingdom of Saudi Arabia. This article has been cited by other articles in PMC. Abstract Immunoassays are bioanalytical methods in which the quantitation of the analyte depends on the reaction of an antigen analyte and an antibody. Immunoassays have been widely used in many important areas of pharmaceutical analysis such as diagnosis of diseases, therapeutic drug monitoring, clinical pharmacokinetic and bioequivalence studies in drug discovery and pharmaceutical industries. The importance and widespread of immunoassay methods in pharmaceutical analysis are attributed to their inherent specificity, high-throughput, and high sensitivity for the analysis of wide range of analytes in biological samples. Recently, marked improvements were achieved in the field of immunoassay development for the purposes of pharmaceutical analysis. These improvements involved the preparation of the unique immunoanalytical reagents, analysis of new categories of compounds, methodology, and instrumentation. The basic methodologies and recent advances in immunoassay methods applied in different fields of pharmaceutical analysis have been reviewed. Principally, these methods are based on a competitive binding reaction between a fixed amount of labelled form of an analyte and a variable amount of unlabelled sample analyte for a limited amount of binding sites on a highly specific anti-analyte antibody. When these immunoanalytical reagents are mixed and incubated, the analyte is bound to the antibody forming an immune complex. This complex is separated from the unbound reagent fraction by physical or chemical separation technique. Analysis is achieved by measuring the label activity e. A standard curve, which represents the measured signal as a function of the concentration of the unlabelled analyte in the sample is constructed. Unknown analyte concentration is determined from this calibration curve 1. Immunoassay methods have been widely used in many important areas of pharmaceutical analysis such as diagnosis of diseases, therapeutic drug monitoring, clinical pharmacokinetic and bioequivalence studies in drug discovery and pharmaceutical industries 2. The detection system in immunoassays depends on readily detectable labels e. The use of these labels in immunoassays results in assay methods with extremely high sensitivity and low limits of detection 15 , In circumstances whereas the specific measurements of large molecules at the femtomole to attomole level in complex biological matrices is required, no doubt that immunoassays are the methods of choice because of their high specificity and sensitivity 17 - In the early stages of drug discovery and development, particularly during the clinical pharmacokinetic studies for the new drug candidate, screening of large number of samples is required. This can be achieved only by using an analytical method of high throughput 20 - The analysis of complex biological matrices e. Although the developing of a new immunoassay method for an analyte may take months due to the time needed for generating the desired antibody , however, once suitable immunoanalytical reagents become available, the immunoassay method can be established in a time frame that is competitive with chromatographic methods. Furthermore, novel techniques were developed to enable the rapid production of specific antibodies. These techniques resulted in dramatic shortening of the time required for developing of immunoassay methods 26 , These potential advantages of immunoassay methods, in addition to the relatively low cost of the instruments, tools, or the reagents made immunoassays the methods of choice in many areas of pharmaceutical analysis. Antibodies are the key reagents on which the success of any immunoassay depends. The antibodies can be either polyclonal or monoclonal. However, for immunoassay development for pharmaceutical analysis purposes, monoclonal antibodies are more advantageous than polyclonal ones 28 - This is attributed to their higher degree of affinity and specificity towards the analyte. Even that, many successful immunoassays were developed using polyclonal antibodies because it was possible to generate the antibodies with high affinity to the analyte 32 - The signal generating labels in immunoassays include radioactive atoms mostly I, ³H, and ¹⁴C 38 , The use of radioactive labels offers extremely sensitive and quite precise assays, however, they have some drawbacks e. Therefore, alternative non-radioactive labels such as enzymes 40 - 49 , fluorescent probes 50 , chemiluminescent substances 51 - 53 , metals and metal chelates 54 - 57 , and liposomes 58 were introduced. On the basis of

number of publications, enzymes are the most common labels employed in immunoassay methods for pharmaceutical compounds. A potential advantage in the use of enzyme labels for immunoassay is the possibility of the amplification of the signal, and subsequently the potential increasing in the sensitivity of the method. This is beneficial when the original signal is not sufficient to get the desirable sensitivity for the analysis. The matrices used for separation of the immune complexes that formed as a result of immunoanalytical reactions include charcoal 59 , polyethylene glycol 60 , second antibody 61 , microbeads 62 , 63 or the most useful well microwell plates; each well of the plate serves as a separate reaction tube. One component of the reaction analyte or antibody is coated onto the surface of the bottom of the plate wells, and the immune complex is formed on the surface of the wells. The use of these plates facilitates the washing steps, and reagents pipetting, and thus leads to semi-automation of the method 64 , These methods can be performed in either competitive or non-competitive designs. The choice from these designs is based on nature of the analyte, labeling chemistry available and the analytical parameter required from the assay e. Competitive design of immunoassays can be carried out in an antigen-capture or antibody-capture format, depending on whether the solid phase is coated with antibody or antigen analyte , respectively. After equilibration and separation, the label activity on the solid phase is measured, and the measured signal is inversely correlated to the concentrations of analyte in the sample The competition occurs between the analyte in sample and the immobilized analyte for the binding to a limited amount of labelled anti-analyte antibody. After equilibration and separation, the activity of the label bound to the solid support is measured, and the signal is inversely correlated to the concentration of the analyte. It requires two antibodies that bind to non-overlapping epitopes on the analyte molecules. One of the two antibodies is bound to the solid phase, and the second one is labelled and used for detection. The sample analyte is allowed to bind to an immobilized antibody. After washing, the solid support contains the formed analyte-antibody complex is incubated with an excess of the second labelled antibody, which binds to the remaining epitope on the analyte molecule. After washing, the activity of the label bound to the solid support is measured.