CRICH Survey Research Unit

Methodology Bits

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The Epidemiological Ladder Version 2

There are many useful classification frameworks for epidemiological designs and attempts to make the distinctions between these designs easier to understand.[1,2,3,4,5] The Epidemiological Ladder presented here adds to this body of literature by proposing a quick reference guide to six well established epidemiological designs.

DESIGN CHARACTERISTICS	DESCRIPTIVE	ANALYTIC				
		OBSERVATIONAL				EXPERIMENTAL
	CASE REPORT/SERIES	CROSS SECTIONAL	CASE CONTROL	RETROSPECTIVE COHORT	PROSPECTIVE COHORT	RANDOMIZED CONTROLLED TRIAL
Alternative study names	Clinical series	Prevalence study, disease frequency survey	Retrospective/back wards design; case referent; case comparison	Historical prospective; non concurrent cohort; non concurrent prospective, trohoc study	Follow-up study; prospective study; longitudinal; concurrent; incident;	Experimental cohort; randomized comparative trial; intervention trial
Description	Describes the characteristics of a case or a series of cases, looking at outcomes and/or exposures	Estimates the prevalence of an outcome or investigates the relationship between outcome and exposure at a particular point in time	Compares a group with known outcome and suitable group without the outcome to understand the relationship between this outcome and past/current exposure	Collects/reviews retrospective data to compare a group with known exposure and a suitable unexposed group to examine the relationship between exposure and outcome incidence	Prospectively follows a group with known exposure and a suitable unexposed group to investigate the relationship between exposure and outcome incidence	Randomly allocates participants/units into exposed and unexposed groups and prospectively follows these groups to investigate the relationship between exposure and outcome incidence
Can test a hypothesis	No	Yes	Yes	Yes	Yes	Yes
Samples by or assigns to more than one group	No	No	Yes	Yes	Yes	Yes
Samples by or assigns to exposure	N/A	N/A	No	Yes	Yes	Yes
Follows the development of new outcomes	N/A	N/A	No	No	Yes	Yes
Randomly assigns the exposure	N/A	N/A	No	No	No	Yes
DESIGN QUALITIES						
Sample size	Usually small	Usually quite large	Requires fewer subjects than cross-sectional surveys Can be very large if outcome is binary or rare			
Time and cost	Relatively fast and inexpensive	Quite variable	Relatively fast and inexpensive		Can be very costly and time consuming	
Ethics	Privacy, confidentiality, power relations, risk and benefits considerations					
	Particularly difficult to maintain confidentiality	May be issues regarding access to data				Treatment denial to unexposed and potential harm exposure to exposed
Can estimate prevalence or incidence	Neither	Prevalence only	Neither	Prevalence and incidence	Prevalence and incidence	Can estimate treatment outcomes and adverse events rates
Can establish timing and directionality of events	No				Yes, can establish timing and directionality of events	
Can determine association and causality	No	Only association				Yes, association and causation
Can control for confounders	N/A	Possible unequal distribution of confounders between groups				Usually balanced on known and unknown confounders by randomization, but statistical analysis may also be used to adjust for known confounders
		Yes, by adjusting in analysis, but Information about confounders may not be available or collected	Can be matched on known confounders through matching of cases and controls or by adjusting matching in analysis	Yes, groups can be matched on known confounders through matching exposed and unexposed groups or by adjusting in analysis		
Main parameters of interest	Descriptive statistics	Prevalence, correlation	Odds ratio	Risk ratio, rate ratio, hazards ratio		Mean difference, risk and hazard ratios
Typical analysis strategies	Percentages, mean, standard deviation	95% confidence interval, linear and logistic regressions	Logistic regression, *t* test, χ^2	Log-binomial, Poisson and Cox regressions, *t* test, χ^2		Analysis of covariance, log-binomial and Cox regressions

The main differences among six basic epidemiological designs

Case Report/Series describe the characteristics of a case or a series of cases, looking at outcomes and/or exposures. One main difference between case report/series and all the other basic epidemiological designs is that they are descriptive studies while all the other designs are or have the potential to be analytic studies. Cross sectional studies can be both, descriptive or analytic. One main difference between case report/series and descriptive cross sectional studies is that case report/series usually collects information on a small number of cases and cannot estimate prevalence, while cross sectional studies can. Example: A case study published on The Lancet in 1983 led to further investigation of the relationship between AIDS and blood transfusion. The study described a single case of an infant who received multiple transfusions during the first few days of life and subsequently developed unusual repeated infections. The child clinical picture was suggesting AIDS, but there was no family history of immunodeficiency. After further investigation it was determined that one of the blood donors have died of AIDS.[6]

Cross Sectional Studies are commonly designed to estimate the prevalence of an outcome. Analytic cross sectional studies test a hypothesis and can determine association between exposure and outcome, but cannot establish causality. Exposure and outcome data are sampled at the same time from the same population. Example: The Canadian Community Health Survey (CCHS) is a good example of a well-known cross sectional study. The CCHS is a cross-sectional survey that collects information related to health status, health care utilization and health determinants for the Canadian population at the sub-provincial levels of geography (health region or combined health regions). A multi-stage sample allocation strategy is utilized to collect information from a sample of 65,000 respondents on an annual basis.[7]

Of all the basic epidemiological designs, the **case control study** is the only one that samples the population by outcome. It compares a group with a given outcome (the cases) and suitable group without the outcome (the controls) to understand the relationship between the outcome and past or current exposure. Example: The association between exposure to asbestos (set of natural minerals) and pleural mesothelioma (form of cancer) was documented by a number of case-control studies in different parts of the world. For example, a French hospital-based study was published in the American Journal of Epidemiology in 1998. The team interviewed 405 cases and 387 controls about their job histories to determine cumulative exposure to asbestos and found a clear dose-response relation between cumulative asbestos exposure and pleural mesothelioma.[8]

Retrospective Cohort Studies collect/review retrospective data to compare a group with known exposure and a suitable unexposed group to examine the relationship between exposure and outcome incidence. It is the only design that samples by exposure and tests the relationship between exposure and outcome after both of them have already manifested. Mortality studies are common within retrospective cohorts. For example: a mortality study published in 1984 was conducted at a nickel company in Canada compared employees observed number of deaths to their expected number of deaths based on rates for the region. Among other findings, sinter plant workers showed a significant increase of cancer deaths.[9]

Prospective Cohort Studies prospectively follow a group with known exposure and a suitable unexposed group to investigate the relationship between exposure and outcome incidence. Prospective Cohort studies and Randomized Controlled Trials are the only basic epidemiological designs that follow the development of a new outcome in real time. This is a very important characteristic since it makes it possible to establish the timing and directionality of events. Example: The Framingham Heart Study is a classic cohort study example carried out in Framingham, Massachusetts (USA). This is a long-term, ongoing cardiovascular study of the town residents of Framingham that began in 1948 with 5,209 adult subjects and is now on its third generation of participants. Study milestones include the strong link between hearth disease and smoking, diet and exercise.[10]

Randomized Controlled Trials randomly allocate participants into exposed (treatment) and unexposed groups, and prospectively follow these groups to investigate the relationship between exposure and outcome incidence. This design is considered the only main epidemiological design that can prove causality. Differently from prospective cohort studies, the random allocation of participants tends to balance known and especially unknown pre-randomization factors in both groups and eliminates confounding. Example: The At Home/Chez Soi study is a good example of a Canadian national level clinical trial that had recent impact on policy. The first phase of the study randomized 2,148 participants experiencing mental health and homelessness into treatment and treatment as usual groups as a way to compare the groups receiving the Housing First approach versus the group of people receiving usual care.[11]

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