Radiation epidemiology: concept, methodology and statistical resources

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Abstract. As radiation exposure is the main point of interest in radiation epidemiology, epidemiologists try to relate the risk of diseases (mainly the risk of cancer) to the different levels and patterns of humankind exposure to radiation. Statistics as a branch of mathematics is able to prove associations and infer causality. As many researches are object of methodological limits, mainly those related to both the insufficient size of the sample and descriptive analysis as well as the choice of methods and variables, this paper aims at describing firstly the main kinds of epidemiological studies. Secondly, it relates distributions and summary measures (central tendency measures, measures of dispersion and normal distributions) and hypothesis tests as well necessary for each study. It also discusses the most appropriate statistical resource to the epidemiological evaluation. Finally, the main aim of this study is both to elaborate a systematic review of the researches that have been already done in Brazil since 2000, focusing on the effects caused by the occupational exposures to ionizing radiation in order to establish positive associations between them and to analyze the risk related to the workers health. This paper has as its basis the Reports in Public Health (Public Health Books-CSP) from which several studies about the exposure effects to ionizing radiation and referred kinds of cancer (e.g.: leukemia, skin cancer, thyroid gland cancer and bone cancer) have been taken as object of analysis. The relevance of this study lies in the most applied methods of risk to establish positive associations in ionizing radiation, in the relation between workers' workplace and his health.

KEYWORDS: Epidemiological studies; risk analysis, radiation epidemiology, association measures.

1. Introduction

Epidemiology is the study of the distribution and determinants of disease prevalence in man. In radiation epidemiology, exposure to radiation is the factor of primary interest, and epidemiologists seek to relate risk of disease (primarily cancer) to different levels and patterns of radiation exposure [1].

Epidemiological research may be divided into two parts: the first one is due to radiation exposure, implying the risk factor and is accomplished by association measures; the second one is essentially based on causal thought, the risk factor being its cause that needs the quality of scientific evidence, privileging some inferential criteria [2].

For the judgment of causality, the following criteria may be considered: intensity of association, right chronological sequence, statistic significance, dose-response effect, consciousness and specificity of association.

This work's main interest is to approach calculation forms to detect ionizing radiations and the possible interpretation of association measures to the results of the analysis.

The principal aim of this work is to present a survey of the types of epidemiological studies related to association measures, significance of statistical measures and the implications of calculation forms, considering the risks of exposure to ionizing radiations and the possible interpretation of the association measures in the results of the analysis.

The design of an epidemiological study must assume comparability in the selection of study participants, comparability in the collection of exposure and disease information relevant to each study subject, and comparability of the basic characteristics of the study subjects. Lack of comparability in

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any epidemiologic study may undermine inferences about an association between exposure and disease, i.e. may lead to one or another form the bias, so that interpretation is ambiguous or impossible.

Three common and potentially serious forms of bias are selection bias, when enrollment into a study is dependent on both radiation exposure and disease status; information bias, when information on disease or on radiation exposure is obtained differently from exposed or from disease persons and confounding bias, when a third factor exists that is related to both radiation and disease effects confounding bias [1].

2. Types of epidemiological studies

Research studies are often classified as experimental or observational, depending on the manner in which the levels of the explanatory factors are determined. When the levels of at least one explanatory factor are under the control of the investigator, the study is said to be experimental. When the levels of all explanatory factors are determined by observation only, the study is observational. The majority of studies relevant to the evaluation of radiation risks in human population are observational [1].

Two basic strategies are used to select participants in an observational epidemiological study that assesses the association between exposures to radiation and disease: select exposed persons and look at subsequent occurrence of disease, or select diseased persons and look at their history of exposure.

A fundamental issue in epidemiology is its methodological conceptualization, its sub-classifications, its advantages and disadvantages and its limitations, as presented in Table 1.

Table 1: Types of epidemiological studies, sub-classification, advantages, disadvantages and types of analysis [2].

Types of epidemiologic studies	Sub-classification	Vantages	Disadvantages	Forms of analysis
Ecological	Territorial Studies(quality of life)/ Institutional aggregate studies (partial risks)	Facility of execution; relative low cost/analytical simplicity/ capacity to generate hypotheses	Low analytical potential/low development of data analysis techniques/vulnerable	Graphic analysis/ indicator comparison/ linear correlation analyses (uni-variate and multivariate)
Cross-sectional	Group studies/ inquires/ special population studies(school children, old people), Domiciliary identification/multiphase studies	Low cost/high descriptive potential (subsidy to planning), analytic simplicity	Vulnerable to biases (especially to selection) low analytical potential (inadequate to test causal hypotheses	Comparison of health and exposition indicators/ statistic significance test
Cohort	Follow up stable cohort and dynamic cohort/ Non concurrent	Produces direct risk measures/high analytical potential/design simplicity	Vulnerable to losses inadequate to low frequency diseases/ relative high cost	Relative risk calculation/ attributable risk/people/year (dynamic cohort study
Case control	According to Group disposition: Paired and Non-paired According to case origin: prevalent and incident	Relative low cost/ high analytical potential/ Adequate to the study of rare diseases.	Unable to estimate risk (reduced descriptive potential) vulnerable to many biases (selection)/ analytical complexity	Relative risk estimate ”Odds Ratio”/ attributable risk Levin’s percentage

2.1 Association Measures

Association measures aim at evaluating the coincidence of a given pathology (or any health occurrence) in the presence of a condition hypothetically attributed to a risk factor. The totality of association measures is the answer to the following question: "Under which conditions does this disease occur? In other words: is there a real association between factor Z and the disease X"? These indicators measure the power or amplitude of an association among epidemiological variants, in other words, they are the agents of epidemiological analysis.

There are two kinds of association measures: proportionality measures (such as mean ratio and correlation, prevalence ratio, relative risk (RR) and Odds Ratio (OR) and the measures of difference association that are attributable risk (AR) and Levin's AR attributable risk to the population (ARP %).

As the importance of this work is due to the most used risk methods, it will focus on the association measures, their importance in the analysis of quantitative data and in the comparison with other Brazilian studies, since 2000. This work approaches the effects of exposure to ionizing radiation on people, including the most common types of cancer, the most observed cases, the most evidential studies and the association measures applied.

The analysis of epidemiological data becomes more complete and useful in the prevention of diseases when we relate the kind of epidemiological study, using the calculation and interpretation of the three types of measures: occurrence measures, association measures and significance measures. Thus, each type of measure has its features, and each one is listed in Table 2.

Table 2: Scheme for the analysis of epidemiological studies [2]

Type of Study	**Occurrences**	**Measures of Association**		**Measure of Significance**
		Proportionality	**Difference**	**Statistics**
Ecological	Means/ frequencies	Means ration ratio/correlations	-	Means difference test (*Z* and *t*) Correlation significance test
Cross-sectional	Prevalence	Prevalence ratio	Prevalence difference (PD)	Proportion difference test (*Z* and *t*) Qui-square test (x^2)
Cohort	Incidence	Relative risk (RR)	Attributable risk (AR, RAP %)	Qui-square test (x^2)
Case-control	_	Odds ratio (OR)	Levin's AR (RAP %)	Qui-square test (x^2) Mantel- Haenszel (MH x^2)

Having assessed whether or not there is evidence of an association between radiation exposure and a disease in the population of interest, the next task is to assess whether noncausal factors may have contributed to the association. An association, might not represent a causal link between radiation and disease, but rather could be due to chance, bias or error [1].

2.2 Statistical Inference

Statistical inference may be defined as the extraction of data from quantitative or qualitative information, using statistical methods to describe and to use it in order to test adequate hypotheses [3].

Association measures resulted from the study analysis will not be valid for the hypothesis test, if they do not control the influence of variations foreign to the association which are capable of confounding

and modifying them. The study of cause-effect relation in epidemiology starts from the objective of estimating an effect measure (risk) between exposure and disease. In this process, the identification of the interaction between the causes and the confounding factor is fundamental [4].

Confounding is the phenomenon whereby a third variable (the confounder) alters the estimate of an association between a presumed antecedent facto and a disease. It can occur when the selection of subjects (cases and controls in a case-control study or exposed an unexposed in a cohort study) depends in some way upon the third variable, possibly in a manner unknown to the investigator. Variables associated only with exposure or diseases are not confounders. To be a confounder a variable must beet three conditions: it must be a risk factor for the disease; it must be associated with the exposure in the study population and it must not be in the causal pathway from exposure to disease [5].

Although there are many procedures to estimate relative risk by stratification, controlling the confounding variable effect, the Mantel-Haenszel method was the first one and the most used in research [6].

The statistical tests estimate the probability of the detected effect to have occurred by chance and they permit for the researchers to compare parameters such as means and proportions, and to determine if the difference between them is statistically significant to establish the critical ratio.

To choose the adequate significance test for the epidemiological design, one should consider the types of variables, the types of analysis and the measures of association.

The most advanced inferential statistics programs include the Qui-Square test (x^2), the differences among proportions test (Z), difference among means test (t), Pearson's r significance test, Spearman's r significance test, x^2 Mantel Haenszel, F (isolated and combined effects), ANOVA, ANCOVA, multiple linear regression and other multivariable procedures such as logistic regression, log-linear analysis and the discriminant function analysis [7].

2.3. Tools of data analysis

This study included a bibliographical survey in books, bulletins of public health and access to health information systems, from January 2000 to December 2007, aiming at visualizing a general theory for scientific investigation, in other words, an epidemiological methodology for the formulation of hypotheses to be validated in search of solutions to the detected problems.

Many documents were analyzed among them normative and technical documents, legislation documents of regulatory departments such as the Brazilian Nuclear Energy Commission (CNEN) that recommends the principles of radiological protection and exposure to ionizing radiation. [8-13].

The access to health information systems was obtained by internet and the morbidity and mortality estimates from the National Cancer Institute [14].

The information used in the study was obtained in articles, dissertations, academic theses that evaluated ionizing radiation exposure and the health workers.

The research was selected according to these themes: worker's exposure to ionizing radiation in their working place and the development of cancer.

The many studies consulted permitted the verification of which association measures were used, which kinds of epidemiological studies, and the importance to this study of the association measures and how these measures are calculated and interpreted and which types of cancer are more frequently detected due to X-ray and gamma rays ionizing radiation.

3. Results and Discussion

In this study 11 publications were selected and evaluated including six articles, two dissertations and three theses [15-25].

Articles: Systematic Mass Abreugraphy: economically non viable technique, offering danger due to radiation exposure (2006); Chromosomic alterations caused by radiation from computer monitors (2002); Radiation exposure during pre-birth period (2001); An educational sensitization practice to ionizing radiation affecting health workers (2006); Evaluation of the occupational risks affecting radiology workers (2005); Ionizing radiation and the observation of the Conselho Federal de Enfermagem (Federal Nursing Council) resolution – COFEN (2005).

Dissertations: All dissertations were presented at the University of São Paulo. Goiania Revisited: recent measures of environmental ionizing radiation (2003) and Occupational activity, oral cavity and oropharynx cancer (2004).

Theses: Occupational risks related to pharyinx cancer: a case control study (2003); Standard mortality rate in a historic cohort of workers exposed to Radon in underground coal mine, Paraná – Brazil (2006); Ionizing radiation: mass dosimetry (2003), post-doctorate dissertation.

In the present study the association measures between radiation exposure and disease were carried out. The association measures mostly used were: Relative Risk (57%), Odds Ratio (29%) and means (14%) because they were more adequate to this study.

The kinds of epidemiological studies mostly used were: cohort studies, case-control studies and socio demographic survey.

The main inference methods used were: T Student, Logistic Regression Analysis, comparison among proportions and, in 50% of the cases, the p value and the 95% confidence interval were considered. The Monte Carlo inference method was used in the Post-doctorate dissertation. Statistic inference permits the evaluation and estimate of the model to predict, generalize and to make future inferences.

4. Conclusion

The essential feature of data collection, analysis, and interpretation in any science is comparability. The methods used to measure exposure to radiation and to measure disease must be comparable, the analytical techniques must ensure comparability, and the interpretation of the results of several studies must be based on comparable data.

The information obtained in the present study, taking into account the literature survey on epidemiological studies, made it possible to characterize the sub-classifications, the advantages and disadvantages and forms of analysis in each epidemiological design.

For the analysis of the evaluation methods of exposure, a fundamental step in any epidemiological study, a comparison among the occupational and disease occurrence was necessary.

The data analysis showed that leukemia, skin cancer, breast cancer, thyroid cancer and bone cancer are the types of cancer mostly detected X-ray exposition or to any other source of ionizing radiation. However the material observed did not permit to identify of the ionizing radiation exposure and the development of cancer, this was not the aim of this study.

Finally the inference methods can optimize the effectiveness of statistics and produces significant statistic results.

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