

## A Case Report on Neuroepidemiology

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### Abstract

Neuroepidemiology is a translational science based on the use of epidemiologic data in the domain of neurological and psychiatric diseases. The epidemiological data have the goal of understanding the causes of disease collecting information on new cases of disease (incidence) and evaluating the consequence of disease using information on new and old cases (prevalence) estimating the burden of disease. The unifying concept in epidemiology is the construction of appropriate analytic methods to elaborate heterogeneous and complex data with construction of the proper study design, techniques to estimate the links between causes of diseases and disease onset and frequencies, taking into account possible factors that may distort or induce changes in the estimates (confounding and interaction). In this article, we analyze the pros and cons of all the main study designs to determine frequencies, association and causes of disease: cohort studies, case-control, prognostic studies and randomized clinical trials. We analyze also a particular study design as the case cross-over study.

**Keywords:** Neuroepidemiology; Cohort studies; Case control; Registries; Neurodegenerative diseases

### Introduction

The Neuroepidemiology Unit is an intellectual community of faculty and students in the Department of Epidemiology who share an interest in understanding the causes, origins, progression, and consequences of neurological disorders. Our research focuses on a wide range of brain-related disorders, from neurodevelopmental disorders of early life through neurodegenerative disorders of aging. Students have an opportunity to engage with faculty who are leading scholars in the epidemiology of epilepsy, Alzheimer's disease, cerebrovascular disease, Down syndrome, and other neurological disorders [1]. Much of our work also focuses on understanding the complex genetic contributions to these disorders, including use of family studies and statistical genetic methods to identify specific genetic variations that contribute to risk, and study of the psychosocial impacts of these gene discoveries on affected persons and their families [2]. Within the Department of Epidemiology, we are closely affiliated with the Psychiatric Epidemiology Unit, and this connection is recognized by a series of joint seminars organized by both units together. Neuroepidemiology is a science of incidence, prevalence, risk factors, natural history and prognosis of neurological disorders, as well as of experimental Neuroepidemiology, which is research based on clinical trials of effectiveness or efficacy of various interventions in neurological disorders.

### The scopes of Neuroepidemiology

Neuroepidemiology investigates risk and protective factors that may exert their effect directly on the underlying neuropathology's of diseases or that may influence the clinical expression of signs and symptoms in the presence of damage. In the former case, modulation of risk exposure is ultimately concerned with avoidance of disease, and can be conceived as primary prevention [3]. In the latter case the modification of the risk profile may instead delay (or advance) the actual clinical onset of the disease, which would correspond to secondary prevention. There is very likely a complex interplay between the expression of clinical symptoms and the underlying neuropathology of disease, and empiric evidence may not be easy to reconcile. Here we illustrate the case of dementia, and the transformative relevance of endorsing a life-course approach to improve its study. The relationship between the manifest clinical symptoms of dementia during life and

the underlying pathologic hallmarks of Alzheimer's disease (AD) measured postmortem varied markedly in a large representative sample of community-dwelling elders, particularly at older ages. More recent studies have used functional and structural brain imaging techniques to quantify beta-amyloidosis and neurodegeneration in individuals without cognitive impairment [4, 5].

The two most frequently used study approaches in epidemiologic analysis include cohort and case-control studies. Choice of these study designs is generally dictated by several factors, including the particular study question; the exposure frequency; the prevalence or incidence of the illness; and logistics. In a cohort study, subjects are classified on the basis of presence or absence of exposure to a particular factor, and then followed in time to assess the development of disease [6]. Cohort studies may be either prospective (following subjects actively forward in time) or retrospective (where the outcome of interest has already occurred, and all of the follow-up has occurred in the past and all information is historical). Cohort studies are most useful to study common outcomes that may occur within short periods of time, or to study outcomes following a rare exposure. Cohort studies are useful in documenting the natural history of disease, and identifying particular risk factors for illnesses; population-based cohort studies may allow for determining incidence and prevalence of a disease [7].

### Factors influencing the epidemiology of viral CNS disease

There are several key factors that influence the epidemiology of viral infections of the nervous system. Of critical importance is the host-agent relationship, which is dependent upon various features and characteristics of both the infecting agent, as well as the

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particular properties or characteristics of the person who is infected (host). Both of these factors influence the occurrence and pattern of human infections, and need to be considered in tandem. Various features of the infecting agent may influence the occurrence of disease [8]. Infectiousness describes the relative ease or difficulty by which an agent may be transmitted to other hosts; respiratory or droplet-spread agents tend to be more infectious than those spread by close person-to-person contact, for instance. Infectivity relates to the ability of an infectious agent to enter, survive, and multiply in a host, and is generally estimated by assessing the number of hosts infected in the context of the number of susceptible and exposed individuals. Pathogenicity is the ability of an agent to cause clinical disease in a host once infection occurs; although this is in large part related to specific characteristics of the infectious agent, host susceptibility may also play a large role in pathogenicity. Similarly, virulence refers to the relative severity of infection caused by a pathogenic agent, and refers to the numbers of serious or disability-producing infections compared to the total number of infected persons. Immunogenicity is the ability of an infecting agent to stimulate an immunologic response in the host; this in part determines the pathogenicity and virulence of a particular agent, and is an important determinant of whether infection confers long-lasting immunity to the agent [9]. Nearly all of these agent factors are substantially influenced by concomitant host factors. For instance, the pathogenicity of a particular agent may be greatly increased in persons with particular risk factors, such as weakened immunity or extremes of age. The virulence of a particular agent may similarly be influenced by particular host risk factors [10].

### Aseptic meningitis

Aseptic meningitis is commonly defined as a syndrome consisting of acute onset of meningeal signs and symptoms, CSF exocytosis, and absence of microorganisms on Gram stain or culture [11]. Clinically, aseptic meningitis presents with the abrupt onset of fever, headache, and meningeal signs, including nuchal rigidity, photo- or photophobia, and nausea/vomiting. CSF is characterized by a moderate exocytosis and elevation in protein, but negative bacterial studies [12]. It is characterized by a relatively benign clinical course, and the absence of features of encephalitis or myelitis [13]. Like encephalitis, there are numerous etiologies of aseptic meningitis, including toxic, immune-

mediated, neoplastic, and chemical causes, as well as a host of infectious pathogens. However, the most common causes of aseptic meningitis are viral etiologies [14-15].

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