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Validity of dementia and Alzheimer's disease diagnoses in Finnish national registers

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Abstract

Background: We investigated dementia and Alzheimer disease (AD) diagnoses in three national registers in Finland: the Hospital Discharge Register (HDR), the Drug Reimbursement Register, and the Causes of Death Register (CDR).

Methods: The Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study was used as the gold standard. Participants were first evaluated in 1972 to 1987, and were reexamined in 1998 and in 2005 to 2008.

Results: Two approaches were used for the HDR: with a time restriction (considering "positive" only those cases recorded in the HDR before CAIDE study evaluations) and without a time restriction. Sensitivity of the HDR was 13.7% with time restriction and 51% without time restriction (dementia), and 15.6% with time restriction 55.6% without time restriction (AD). The positive predictive value (PPV) was 87.5% with time restriction and 96.3% without time restriction (dementia), and 100% for AD. Sensitivity and PPV of the HDR were greater after 1998. For AD in the Drug Reimbursement Register alone, sensitivity was 63.5% and PPV was 97.1%; together with the HDR, sensitivity became 65.4% with time restriction and 71.1% without time restriction, and PPV was 100%. For dementia in the CDR, sensitivity was 62.2% and PPV was 100%.

Conclusions: Diagnoses in registers have very good accuracy, but underestimation of dementia/AD occurrence may cause an underestimation of associations with risk/protective factors.

Keywords: Dementia; Alzheimer disease; Diagnosis; Population-based registers; Epidemiology

1. Introduction

Compared with cardiovascular disease prevention, dementia prevention is a newer field of research, in which the idea of modifiable risk factors began to receive more intensive attention only by the end of the 1990s. Current data from epidemiologic studies indicate that dementia, cardiovascular disease, stroke, and diabetes mellitus—all major public health problems—share several risk and protective factors [1].

Many methodological issues are yet to be addressed before formulating dementia prevention guidelines [2]. Dementia is a syndrome that occurs later in life, but the underlying brain pathologies (of which Alzheimer's disease [AD] and vascular disease are most common) can take decades to develop. Effective dementia prevention is thus dependent on switching from a late-life to a lifelong approach. However, few long-term population-based studies starting at midlife are currently available [2]. In addition, identifying dementia-related diseases is a time- and resource-demanding process, usually involving several steps, including population screening, clinical evaluation, and differential diagnosis investigations. Population-based

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registers can be an efficient, alternative way to identify patients, and this approach has been used successfully in other fields such as cardiology, diabetes, stroke, or oncology. Because disease misclassification in registers is always a concern, it is important to investigate the validity of register diagnoses against diagnoses made in high-quality population-based studies. This has been seldom done for dementia [3–5].

The Finnish survey database for monitoring of risk factors for chronic diseases (FINRISK) consists of large population-based surveys carried out since 1972 every 5 years using independent, random, and representative population samples from different parts of Finland [6]. The age range for each survey is 25 to 75 years. The first surveys during the 1970s and 1980s were conducted within the North Karelia Project [7] and FINMONICA component of the World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (WHO MONICA) Project [8]. Parts of the 1972 to 1987 cohorts were investigated further after 1998 in the Cardiovascular Risk Factors, Aging and Incidence of Dementia (CAIDE) study [9]. The FINRISK database is linked regularly to national registers such as the Hospital Discharge Register (HDR) and Causes of Death Register (CDR), as well as to the Drug Reimbursement Register. The overall quality of the Finnish HDR is commonly regarded as high, and its validity has been evaluated for several diagnoses (i.e., coronary heart disease or stroke [10,11]), but not for dementia. The current study aims to investigate the validity of dementia and AD diagnoses in the registers by using data from the CAIDE study to determine whether the FINRISK survey database can be used for monitoring risk factors and incidence of dementia/AD.

2. Methods

2.1. CAIDE study

Participants in the CAIDE study were derived from four separate, independent population-based random samples examined within the framework of the North Karelia Project and the FINMONICA study in 1972, 1977, 1982, or 1987 (baseline visit) [7,8]. Participation rates in these surveys ranged from 82% to 90%. A random sample of 2000 persons still alive, age 65 to 79 years at the end of 1997, and living in two geographically defined areas in or close to the cities of Kuopio and Joensuu, was invited for a first reexamination carried out in 1998. A total of 1449 individuals (72.5%) participated, including 900 women (62.1%). A second reexamination of the CAIDE sample was done between 2005 and 2008. Of the initial 2000 persons, 1426 were still alive and living in the region in the beginning of 2005, and 909 (63.7%) participated, including 590 women (64.9%). The mean age ± standard deviation was 50.6 ± 6.0 years at baseline, 71.3 ± 4.0 years at the first reexamination, and 78.6 ± 3.7 years at the second reexamination.

The survey methods used during the baseline visit were standardized carefully and they complied with international recommendations. The surveys in 1982 and 1987 followed the WHO MONICA protocols, and the methods used in 1972 and 1977 were comparable. During the first and second reexaminations, methods were similar to those applied in previous surveys. In addition, cognitive status was assessed with a three-step protocol: a screening phase, a clinical phase, and a differential diagnostic phase. In 1998, participants who scored $\leq$24 points on the Mini-Mental State Examination (MMSE) [12] at the screening phase were referred to the clinical phase for further evaluation. In 2005 to 2008, new cognitive tests were added to the screening phase to increase sensitivity to milder forms of cognitive impairment. Subjects with $\leq$24 points on the MMSE, or with a decline of $\geq$3 points on MMSE compared with the first reexamination, or with less than 70% delayed recall in the Consortium to Establish a Registry for Alzheimer's Disease word list [13], or with a serious informant concern regarding the participant's cognition were referred to the clinical phase. During both reexaminations, the clinical phase included detailed neurological, cardiovascular, and neuropsychological examinations, and the differential diagnostic phase consisted of brain imaging (magnetic resonance imaging/computed tomography), blood tests, and, if needed, cerebrospinal fluid analysis, and an electrocardiogram. A review board, including the study physician, study neuropsychologist, and a senior neurologist, ascertained the primary diagnosis based on all available information. Dementia was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, criteria [14], and AD was diagnosed according to the U.S. National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association criteria [15]. The CAIDE study was approved by the local ethics committee, and written informed consent was obtained from all participants.

For the validation of register data on dementia and AD diagnoses, 103 CAIDE participants were excluded from the analyses. Of these, 97 (40 in the 1998 visit and 57 in the 2005 to 2008 visit) had been referred for further evaluations after the screening phase but did not participate in the clinical phase. For the remaining 6 participants, the review board reported some difficulties in reaching an agreement on diagnosis. Of the 1505 CAIDE study participants, 744 were present at both reexaminations and, of these, 51 were diagnosed with dementia (six in 1998 and 45 in 2005–2008), of which 45 had AD (five diagnosed in 1998 and 40 in 2005–2008). A group of 659 subjects participated in the first reexamination only, and 49 were diagnosed with dementia (38 with AD). The remaining 102 subjects participated in the second reexamination only (17 dementia cases, of which 12 had AD).

2.2. The National Hospital Discharge Register

The HDR is maintained by the National Institute for Health and Welfare. It includes information on inpatient