**Supplementary Material**

**Antiepileptic Drug Use Is Associated with an Increased Risk of Pneumonia Among Community-Dwelling Persons with Alzheimer’s Disease-Matched Cohort Study**

**Supplementary Table 1.** Data sources and definitions for baseline covariates.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **Classes/ definition (ATC code, ICD-10 codes, NOMESCO codes)** | **Measurement point** | **Data source** | |
| **Sociodemographic** | | | |
| Age, years | -64  65-74  75-84  85- | Baseline | PR | |
| Gender | Male  Female | Baseline | PR | |
| Occupational socioeconomic position | High  Medium  Low  Unknown | Highest position recorded in the middle age (45-55 years) | SF | |
| **Other medication use at the baseline** | | | |
| Antipsychotics | N05A excluding lithium N05AN01 | Within 30 days before start of follow-up | PR | |
| Antidepressants | N06A | Within 30 days before start of follow-up | PR | |
| Benzodiazepines and related drugs | N05BA, N05CD, N05CF | Within 30 days before start of follow-up | PR | |
|  |  |  |  | |
| PPI use | A02BC | Within 30 days before start of follow-up | PR | |
| Oral glucocorticoids | H02AB | Within 30 days before start of follow-up | PR | |
| Opioids | N02A | Within 30 days before start of follow-up | PR | |
| NSAIDs | M01A excluding glucosamine | Within 30 days before start of follow-up | PR | |
| **Previous use of medications** | | | |
| Antiepileptics | N03A | Ever before the washout period (since 1995 until one year before start of follow-up) | PR | |
| **Comorbidities** | | | |
| Coronary artery disease | Hospitalization (ICD-10 I20-I25; NOMESCO FNA, FNC, FNE, FNG00, FNG10, FN1AT, FN1BT, FN1YT) or special reimbursement of coronary artery disease (classification numbers 206, 213, 280) | Diagnosed since 1996 until the start of follow-up (hospitalization); or since 1972 until the start of follow-up (special reimbursement) | SR, HR | |
| Diabetes | Special reimbursement for diabetes (classification number 103) or A10A (excl. A10BX01) use | Diagnosed since 1972 until the start of follow-up (special reimbursement); since 1995 until the start of follow-up (drug use) | SR, PR | |
| Asthma/ COPD | Special reimbursement (classification numbers 203) or hospitalization (ICD J44-J46) | Diagnosed since 1972 until the start of follow-up (special reimbursement); since 1996 until the start of follow-up (hospitalization) | SR, HR | |
| Rheumatoid arthritis | Hospitalization (ICD-10: M05, M06, M45) or special reimbursement (classification number 202) | Diagnosed since 1972 until the start of follow-up (special reimbursement); since 1996 until the start of follow-up (hospitalization) | HR, SR | |
| Previous pneumonia | Hospitalization (ICD-10: J100, J110, J12, J13, J14, J15, J16, J18) | Diagnosed since 1996 until one year before start of follow-up | HR | |
| Previous fracture | Hospitalization (ICD-10: S\*2, T02\*) | Diagnosed since 1996 until the start of follow-up | HR | |
| Epilepsy | Special reimbursement (classification number 111) | Diagnosed since 1972 until the start of follow-up | SR | |
| Any previous cancer | Hospitalization (ICD-10: C00-C97, Z85) | Diagnosed since 1996 until the start of follow-up | HR | |

AD, Alzheimer’s disease; ATC, Anatomical Therapeutic Chemical; COPD, chronic obstructive pulmonary disease; HR, Hospital Discharge Register; ICD, International Classification of Diseases; NOMESCO, The Nordic Medico-Statistical Committee (classification of surgical procedures); PR, Prescription Register; SF, Statistics Finland; SR, Special Reimbursement Register.

**The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.**

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| --- | --- | --- | --- | --- | --- |
|  | **Item No.** | **STROBE items** | **Location in manuscript where items are reported** | **RECORD items** | **Location in manuscript where items are reported** |
| **Title and abstract** | | | | | | |
|  | 1 | (a) Indicate the study’s design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found | Title p.1, abstract p.2 | RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included.  RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract.  RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract. | p.2 abstract mentions nationwide registers  p.2 country and time frame in the abstract | |
| **Introduction** | | | | | | |
| Background rationale | 2 | Explain the scientific background and rationale for the investigation being reported | p.3-4 |  |  |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | p. 4 |  |  |
| **Methods** | | | | | | |
| Study Design | 4 | Present key elements of study design early in the paper | study cohort p.5 |  |  |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | study setting p.6-7 |  |  |
| Participants | 6 | *(a) Cohort study* - Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up  *Case-control study* - Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls  *Cross-sectional study* - Give the eligibility criteria, and the sources and methods of selection of participants  *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed  *Case-control study* - For matched studies, give matching criteria and the number of controls per case | p. 5 study cohort, p. 6-7 study setting  p. 6-7 study setting | RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided.  RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided.  RECORD 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage. | p. 5 study cohort  p. 5 study cohort  p. 5 registers |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. | p. 6-8, Supplementary Table 1 for diagnostic codes | RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided. | p. 6-8, Supplementary Table 1 for diagnostic codes |
| Data sources/ measurement | 8 | For each variable of interest, give sources of data and details of methods of assessment (measurement).  Describe comparability of assessment methods if there is more than one group | p. 7-8 covariates, Supplementary Table 1 |  |  |
| Bias | 9 | Describe any efforts to address potential sources of bias | p. 6-7 study setting, p. 8-9 statistical analyses |  |  |
| Study size | 10 | Explain how the study size was arrived at | p. 6-7 study setting, Fig. 1 |  |  |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | p. 7-8 covariates, Supplementary Table 1 |  |  |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding  (b) Describe any methods used to examine subgroups and interactions  (c) Explain how missing data were addressed  (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed  *Case-control study* - If applicable, explain how matching of cases and controls was addressed  *Cross-sectional study* - If applicable, describe analytical methods taking account of sampling strategy  (e) Describe any sensitivity analyses | a-b) p. 8-9 statistical analyses  c) 7-8 covariates,  d) reasons for end of follow-up p. 8  e) case-crossover p. 9 |  |  |
| Data access and cleaning methods |  | .. |  | RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.  RECORD 12.2: Authors should provide information on the data cleaning methods used in the study. | p.9 (de-identified data on original study cohort was provided for research team, authors had full access to that)  p. 6 exposure |
| Linkage |  | .. |  | RECORD 12.3: State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided. | p. 9 |
| **Results** | | | | | | |
| Participants | 13 | (a) Report the numbers of individuals at each stage of the study (e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed)  (b) Give reasons for non-participation at each stage.  (c) Consider use of a flow diagram | a) Fig. 1, results p. 10-11  b) no non-participation  c) Fig. 1 | RECORD 13.1: Describe in detail the selection of the persons included in the study (i.e., study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram. | p. 6-7 study setting, Fig. 1 |
| Descriptive data | 14 | (a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders  (b) Indicate the number of participants with missing data for each variable of interest  (c) *Cohort study* - summaries follow-up time (e.g., average and total amount) | a) p. 10 results, Table 1  b) covariates p. 8  c) p. 10 |  |  |
| Outcome data | 15 | *Cohort study* - Report numbers of outcome events or summary measures over time  *Case-control study* - Report numbers in each exposure category, or summary measures of exposure  *Cross-sectional study* - Report numbers of outcome events or summary measures | Table 2 |  |  |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included  (b) Report category boundaries when continuous variables were categorized  (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | a) Tables 2-4,  b) Table 1, Supplementary Table 1  c) Tables 2-3 include incidence rates per 100 person-years |  |  |
| Other analyses | 17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | results p. 10-11, Tables 2-4 |  |  |
| **Discussion** | | | | | | |
| Key results | 18 | Summarize key results with reference to study objectives | p. 12 |  |  |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | p.14 | RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported. | p.14 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | p. 12-13 |  |  |
| Generalizability | 21 | Discuss the generalizability (external validity) of the study results | p.14 |  |  |
| **Other Information** | | | | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | p. 15 |  |  |
| Accessibility of protocol, raw data, and programming code |  | .. |  | RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code. | p. 15 |

\*Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, the RECORD Working Committee (2015) The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Med* **12**, e1001885.

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