

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Cohort profile: The Finnish Medication and Alzheimer's disease (MEDALZ) study
<b>AUTHORS</b>	Tolppanen, Anna-Maija; Taipale, Heidi; Koponen, Marjaana; Lavikainen, Piia; Tanskanen, Antti; Tiihonen, Jari; Hartikainen, Sirpa

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Dr Britta Haenisch German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany
<b>REVIEW RETURNED</b>	27-Apr-2016

<b>GENERAL COMMENTS</b>	<p>The manuscript by Tolppanen et al. is a well written cohort profile describing The Finnish Medication and Alzheimer's disease (MEDALZ) study. Given the need of population-based research in the context of urgent health care problems such as dementia, a register-based nationwide study on medication and Alzheimer's disease (AD) is a valuable tool to examine the use of healthcare service as well as safety and effectiveness of drugs in this patient group.</p> <p>Minor comments:</p> <ul style="list-style-type: none"><li>-In the cohort description the authors mention that physicians also need to confirm whether a patient has other dementing diseases besides AD. I assume those are mixed AD forms. Could you please include (if available) how many of the AD cases are reported as mixed AD.</li><li>-For the limitation section the authors should mention the restriction to AD and mixed AD dementia forms.</li></ul>
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<b>REVIEWER</b>	Heii Arai M.D., Ph.D. Juntendo University, Tokyo, Japan
<b>REVIEW RETURNED</b>	26-May-2016

<b>GENERAL COMMENTS</b>	I am looking forward to seeing your future papers.
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<b>REVIEWER</b>	Chrisitan Lange-Asschenfeldt Department of Psychiatry and Psychotherapa University Hospital of Düsseldorf Düsseldorf, Germany
<b>REVIEW RETURNED</b>	27-May-2016

<b>GENERAL COMMENTS</b>	This cohort provides an unusual high number of participants
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	<p>(essentially a whole country's population) in a „real life“ setting. Such a cohort is of outstanding interest regarding epidemiological questions. Particularly interesting is the opportunity to access patient data before the disease has been diagnosed.</p> <p>The present paper is only a description of the cohort and thus only hints at some problems which are worth analysing, e.g., medication use prior to and during the disease. If such a format is acceptable to the journal there shall be no objections from my point of view and comments are only minor:</p> <p>1) In Table 1, section „... Comorbidities ... Why not break down the F diagnoses found in the sample to diagnostic subgroups, such as affective, anxiety, substance use disorder etc.?</p> <p>2) Abstract, page 2, section „Findings“: the sentence contradicts the statement on page 9, line 8 (regarding the initiation rate of antidepressants: In the abstract, the initiation rate is noted to peak before diagnosis and on p. 9 it peaked six months after the diagnosis).</p> <p>3) Abstract, page 2, para 2, line 4: The word „data“ is missing behind „socioeconomic“.</p> <p>4) Abstract, page 2, para 3, line one: Providing two decimals regarding the average age is not necessary. Second sentence: „The majority...“ instead of „Majority...“</p> <p>5) Page 8, para 3, line 1: „...the cohort“ instead of „...cohort“ and „The majority...“ instead of „Majority...“; line 7: „Approximately one tenth...2 instead of „...tenth...“</p> <p>6) Page 8, para 4, line 3: What does „ADF“ mean?</p>
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### VERSION 1 – AUTHOR RESPONSE

Comments from Reviewer 1 (Dr Britta Haenisch)

Comment 1: In the cohort description the authors mention that physicians also need to confirm whether a patient has other dementing diseases besides AD. I assume those are mixed AD forms. Could you please include (if available) how many of the AD cases are reported as mixed AD.

Response: Yes, this covers also mixed dementia. Unfortunately the Social insurance Institution's reimbursement register has data only on whether the reason for reimbursement was AD or Parkinson's dementia (as these are the only forms of dementia that are eligible for reimbursed medication) so the requested data were unfortunately not available.

Comment 2: For the limitation section the authors should mention the restriction to AD and mixed AD dementia forms.

Response: We have included the following sentences to the limitations section "One limitation of our cohort is that it is restricted to AD cases and mixed dementia cases whose symptoms are deemed to be mainly due to AD. Thus, it does not represent all dementia cases. However, AD is the most common form, accounting for 60-80% of all dementia cases."

Comments from Reviewer 2 (Dr Heii Arai)

Comment 1: I am looking forward to seeing your future papers.

Response: Thank you for this kind comment, we hope our future papers will not disappoint you.

Comments from Reviewer 3 (Dr Christian Lange-Asschenfeldt)

Comment 1: In Table 1, section „... Comorbidities ... Why not break down the F diagnoses found in the sample to diagnostic subgroups, such as affective, anxiety, substance use disorder etc.?

Response: The previous version included schizophrenia, schizotypal and delusional disorders and depression but we have included disorders due to psychoactive substance use, mania and bipolar disorder, neurotic, stress-related and somatoform disorders and disorders of adult personality and behaviour in Table 1 of the revised version.

Comment 2: Abstract, page 2, section „Findings“: the sentence contradicts the statement on page 9, line 8 (regarding the initiation rate of antidepressants: In the abstract, the initiation rate is noted to peak before diagnosis and on p. 9 it peaked six months after the diagnosis).

Response: We have modified the abstract as follows: “The initiation rate of e.g., benzodiazepines and related drugs and antidepressants began to increase already before AD diagnosis”.

Comment 3: Abstract, page 2, para 2, line 4: The word „data“ is missing behind „socioeconomic“.

Response: This has been corrected in the revised manuscript.

Comment 4: Abstract, page 2, para 3, line one: Providing two decimals regarding the average age is not necessary. Second sentence: „The majority...“ instead of „Majority...“

Response: These errors have been corrected in the revised version of the manuscript.

Comment 5: Page 8, para 3, line 1: „...the cohort“ instead of „...cohort“ and „The majority...“ instead of „Majority...“; line 7: „Approximately one tenth...2 instead of „...tenth...“

Response: These errors have been corrected in the revised version of the manuscript.

Comment 6: Page 8, para 4, line 3: What does „ADF“ mean?

Response: This is a typo, which has been revised to “AD” in the revised version.